

Ambient air pollution and cardiorespiratory outcomes amongst adults residing in four informal settlements in the Western Province of South Africa

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(Epidemiology track)

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PART A: PROTOCOL

1. Introduction

The industrial revolution, which spread across the world, transformed societies from being primarily agrarian to relying on technology for mass production. Essential to this revolution was the use of power machines and factories to maximise the number of goods and services provided to communities¹. Despite its many advantages, including; the creation of jobs and the mass production of goods and services to sustain societies, this revolution is also associated with the production of high levels of pollutants²

1.1 Problem Statement

The World Health Organisation (WHO) has estimated that in 2016, 4.2 million deaths were attributed to ambient air pollution. Furthermore, the majority of these deaths occurred in lower and middle-income countries with cardiorespiratory diseases being the main mechanism through which these deaths occurred³.

1.2 Justification

Studies investigating the relationship between air pollution and health outcomes date back to the 20th century^{4,5}. Subsequently, many studies have been conducted to further explore this association. However, most of these studies have been conducted in America, Asia and Europe where air pollution levels and population characteristics differ from those found in Africa and specifically in informal settlements around South Africa⁶⁻¹³. Furthermore, there is a paucity of studies on the continent investigating this relationship, as available studies do not have robust exposure measurements, make use objective outcomes and/or do not control for appropriate confounders (some of which vary across different study population). Moreover, majority of studies from the African continent have focused mainly on children. The proposed study aims to investigate the relationship between ambient air pollution and cardiorespiratory outcomes amongst adults residing in four informal settlements in the Western Province while controlling for relevant confounding variable and will thus contribute to the growing body of literature on this topic on the continent.

1.3 Research Question

What is the association between ambient air pollution and cardiorespiratory outcomes in South African adults in 2016?

1.4 Aim

The aim of the study is to investigate the relationship between ambient air pollution exposure and self-reported cardiorespiratory outcomes amongst adults residing in four informal settlements of the Western Cape

1.5 Objectives

The objectives are:

- To describe the demographics and host characteristics of the study population
- To assess exposure to self-reported indoor and estimated ambient air pollutants of the study participants
- To assess self-reported cardiorespiratory outcomes of the study participants
- To explore potential confounding variables that may be associated with cardiorespiratory outcomes of interest
- To determine the association between exposure to ambient air pollution and self-reported cardio respiratory outcomes

2. Literature Review

The World Health Organisation Air Quality Guidelines have identified four criteria ambient air pollutants that have adverse effects on health. These pollutants include particulate matter (PM), sulphur dioxide (SO₂), nitrogen dioxide (NO₂) and ozone (O₃)¹⁴. Carbon monoxide (CO) has also been shown to have adverse health effects¹⁵.

2.1 Particulate matter

Particulate matter affects more people than any other pollutant and mainly contains: mineral dust, black carbon, ammonia, sodium chloride, sulphate nitrates and water^{16, 17, 18}. Particles of 10 microns or less have the greatest adverse health effect as they are small enough to lodge deep into the lungs¹⁸. The main sources of PM include vehicle emissions, agriculture, power generation and other industrial sources^{14, 19}. PM has also been shown to increase diastolic blood pressure and put the body in an inflammatory and procoagulant state^{20, 21}. Furthermore, PM induces oxidative stress, causes airway irritation by impairing mucociliary and macrophage activity and has been shown to be carcinogenic²².

2.2 Sulphur Dioxide

Sulphur dioxide is a toxic gas with a pungent, irritating and rotten smell. It is mainly derived from fossil fuel combustion at power plants and other industrial facilities^{23, 24}. Smaller sources of SO₂ emissions include industrial processes such as extracting metal ore, the burning of high sulphur containing fuels by vehicles, large ships and non-road equipment. Ecologically, SO₂ emissions are a precursor to acid rain which results in deforestation¹⁴. SO₂ has been shown to reduce cardiac vagal tone (parasympathetic control of the heart) and thus results in increased susceptibility to arrhythmias²⁵. It is also an irritant to the eyes, nose and respiratory tract and causes bronchoconstriction²².

2.3 Nitrogen Dioxide

Nitrogen dioxide is a reddish-brown toxic gas with a sharp, biting odour. It is mainly derived from combustion processes used in the generation of power, heating, ships and vehicles^{14, 26}. NO₂ plays a primary role in the formation of ozone and therefore contributes to the cardiovascular effects of ozone²⁷. It also impairs gaseous exchange and increases bronchial reactivity and susceptibility to respiratory infections²².

2.4 Ozone

Ozone is the most important photochemical oxidant in the troposphere and is formed by photochemical reactions in the presence of precursor pollutants such as Nitrogen Oxides and Volatile Organic Compounds. O₃ has been shown to impair gaseous exchange in the alveoli

and therefore induces increased myocardial stress¹⁴. It also impairs gaseous exchange and induces respiratory tract mucosal inflammation²².

2.5 Carbon Monoxide

Carbon monoxide is a colourless, odorless and tasteless gas that is slightly less dense than air. It is produced from partial oxidation of carbon containing compounds and forms when there is insufficient oxygen to produce carbon dioxide. Its main sources are gas stoves, wood stoves, fireplaces and vehicles²⁸. It is toxic to haemoglobin animals (including humans) at concentrations above 35ppm and causes its harmful health effects by reducing oxygen delivery to the body's organs (including the heart and brain) and tissues²⁹. Acute exposure to carbon monoxide has been associated with headache, dizziness on exertion, nausea and mental confusion. Chronic exposure to carbon monoxide has been associated with flu like symptoms, unconsciousness and death¹⁵.

2.6 Outdoor air pollution and cardiovascular disease in Africa

Ghana and South Africa were included in the World Health Organisation Study on Global Ageing and Adult Health. Analysis of data from the study found that there was a 1.13(95%CI 1.05 to 1.22) increased odds of stroke with each 10 $\mu\text{g}/\text{m}^3$ increase in PM_{2.5}³⁰. In addition, in South Africa, an interquartile increase in PM₁₀ was also found to be associated with a 4.1%(95%CI 0.4 to 8.1) increased risk of mortality attributed to cerebrovascular causes and a 10 $\mu\text{g}/\text{m}^3$ increase in NO₂ was found to be associated with a 3.4%(95%CI 0.3 to 6.6) and 8.0(95%CI 2.9% to 13,4%) increased risk of mortality attributed to cardiovascular and cerebrovascular diseases respectively³¹. Furthermore, in Algeria, it was found that decreasing PM₁₀ annual mean by 5 $\mu\text{g}/\text{m}^3$ would avoid 3 cardiac hospitalisations³²

2.7 Outdoor air pollution and respiratory disease in Africa

In South Africa, a 12 $\mu\text{g}/\text{m}^3$ increase in PM₁₀ and 10 $\mu\text{g}/\text{m}^3$ increase in NO₂ were found to be associated with a 5.5 % (95 CI, 1.4 to 9.6) and 6 % (95%CI 1 to 112.) increase in mortality attributable to respiratory diseases and a cross sectional study conducted in Nigeria found a negative correlation between increasing levels of PM₁₀ and lung function^{31, 33}. Furthermore, in Algeria, decreasing the annual PM₁₀ by 5 $\mu\text{g}/\text{m}^3$ reduced five hospital admissions attributable to respiratory diseases and a study conducted in Namibia also found a significant association between particulate matter and episodes of coughing and phlegm^{32,34}.

2.8 Conclusion

Despite the majority of ambient air pollution related deaths occurring in lower- and middle-income countries, there is a paucity of epidemiological studies investigating ambient air pollution's effect on health in Africa. Furthermore, in addition to the above-mentioned methodological limitations, all but one of the epidemiological studies conducted in Africa investigating the association between air pollution and cardiorespiratory morbidity only made use of particulate matter as an air pollutant. Further research in this field thus needs to be conducted on the continent to not only contribute to the body of knowledge in this field but also to generate information which will assist health authorities to take appropriate measures to promote health on the continent.

3. Methodology

3.1 Study Population and Study Design

This study involved the analysis of a sub-set of data that was collected as part of a larger study conducted in 2016. The larger study was a cohort study investigating the effect of ambient air pollution on asthma among 600 primary school pupils in the Western Cape³⁵. The current study is a cross-sectional study investigating the effect of ambient air pollution on cardiorespiratory outcomes among the guardians of primary school students in the Western Cape. The study areas included informal settlements in three areas prioritised in a needs analysis conducted by the department of Environmental Affairs and Development Planning (DEADP) in 2013. Furthermore, one control area (an area with a low air pollution score ranking) with community members of similar socio-economic status as the three identified areas was identified (Mashipumelel in Noordhoek). These areas were selected to maximise contrasts in exposure levels to the different ambient air pollutants. The exposed areas included an urban industrialised area (Marconi Beam in Milnerton), a peri-urban area with a large informal sector (Khayelitsha) and a rural area (Oudtshoorn).

3.2 Selection of study areas

The selection of study areas in the larger study was informed by a scoring process based on the World Health Organisation's (WHO) Driving Force, Pressure, State, Exposure, effects, Action (DPSEA) framework. This framework aims to integrate health and environment in developing countries dealing with various hazards (e.g. water and food insecurity, HIV/AIDS, malaria etc.) which increases their vulnerability and reduces their ability to cope in situations of environmental pollution exposure.

The scoring process assigned a Total Prioritisation Index (PI) for all the census areas (i.e. statistical data from the census 2011) in the different Districts within the Western Cape. The PI was calculated from an air pollution score, the population density (number of people per square kilometre), total population, and susceptibility and coping score. Hence, an area with poor air quality (but with few people) had a lower score for prioritization compared to an area with similar air quality but with more population density. Details of the prioritization process and methodology have been described elsewhere³⁶. A weighted average was applied to represent the interaction of the various factors to obtain a Total Prioritisation Index as follows:

$$\text{Total Prioritisation Index} = (0.5 * \text{Air Pollution Score}) + (0.1 * \text{population density}) + (0.1 * \text{population}) + (0.3 * \text{Vulnerability Score-susc\&cop})$$

The conclusion drawn from the findings of the Total Prioritization Index across the different municipalities in the Western Cape clearly indicated a significant high intensity of exposure, susceptibility of communities to air pollution, as well as vulnerability, in the City of Cape Town compared to other municipals. The Total Prioritization Index was normalized from 1 to 100, with 100 being the most vulnerable site. However, the selection of an urban industrialised area (Marconi Beam in Milnerton), a peri-urban area (Khayelitsha) and a rural area (Oudtshoorn) was to maximize contrasts between the various areas for various ambient air pollutants and patterns of pollutants.

3.3 Sampling and sample size

In the larger study, a list of all the schools in the study area was obtained from the Department of Education. One or two schools were subsequently located near the City's air monitors. One hundred and fifty Grade 4 students in each study area were targeted. Grade 4 students were targeted because they were old enough to participate in the study and would not leave primary school to enter high school during the study period.

After meeting each school's principal, obtaining permission from the school board and obtaining the grade 4 class lists and addresses, the houses of school children were visited by trained field staff to obtain the caregivers (parent or guardian) consent.

Inclusion criteria for the larger study included: all grade 4 students attending selected schools, all grade 4 students with asthma not selected randomly. Exclusion criteria included: children who had recent operation (within the last 12 months), children who felt like vomiting or had any pain, children with epilepsy, children being treated for Tuberculosis and children with flu, sinusitis or lung infection in the last 3 weeks. The guardians of these children selected in the main study were selected for this cross-sectional analytical study.

Using chi square statistic for comparing two independent samples with the null hypothesis: proportion 1 = proportion 2 and the alternative hypothesis proportion 1 \neq proportion 2 the following outcomes had the following power

For the NO₂ model

- Doctor diagnosis of asthma: using sample size = 572, allocation ratio = 3.2, proportion 1 = 0.0142, proportion 2 = 0.0299; power = 6.45
- Asthma symptom score: using sample size = 572, allocation ratio = 1.4, proportion 1 = 0.0898, proportion 2 = 0.1276; power = 25.09
- Self -reported chest pain: using sample size = 572, allocation ratio = 3.5, proportion 1 = 0.0126, proportion 2 = 0.0441; power = 21.76
- Self -reported hypertension: using sample size = 572, allocation ratio = 1.8, proportion 1 = 0.0488, proportion 2 = 0.0787; power = 21.64
- Self -reported high cholesterol: using sample size = 572, allocation ratio = 2.3, proportion 1 = 0.0142, proportion 2 = 0.0331; power = 6.45

For the PM_{2.5} model

- Doctor diagnosis of asthma: using sample size = 572, allocation ratio = 2.1, proportion 1 = 0.0142, proportion 2 = 0.0299; power = 10.11
- Asthma symptom score: using sample size = 572, allocation ratio = 1.2, proportion 1 = 0.0976, proportion 2 = 0.1197; power = 10.43
- Self -reported chest pain: using sample size = 572, allocation ratio = 2.3, proportion 1 = 0.0173, proportion 2 = 0.0394; power = 16.02
- Self -reported hypertension: using sample size = 572, allocation ratio = 1.3, proportion 1 = 0.0567, proportion 2 = 0.0709; power = 7.4
- Self -reported high cholesterol: using sample size = 572, allocation ratio = 2, proportion 1 = 0.0157, proportion 2 = 0.0315; power = 10.45

3.4 Instruments

3.4.1 Questionnaire

Trained interviewers administered the questionnaires to participants in their spoken language (English, Xhosa or Afrikaans). The principle investigator and study co-ordinator provided training on administration of the questionnaire to the fieldworkers. The questionnaire was back-translated to ensure the consistency and reliability of the questionnaires. The use of mobile technology was implemented in the administration and capture of questionnaires.

The questionnaire used for this study included items on:

- Demographic factors
- Residential History
- Respiratory Health
- Cardiovascular Disease
- Blood Pressure and other chronic illnesses such as high cholesterol
- Occupational History
- Exposure to Indoor Pollutants
- Exposure to Outdoor Pollutants
- Physical Activity
- Psychosocial Stress
- Tobacco Use

Appendix 1 depicts questions asked in each section

The European Community Respiratory Health Survey³⁷ and National Health and Nutrition Examination Survey questionnaire³⁸ was incorporated into the study's questionnaire administered to each grade 4 participant's guardian. From these questionnaires the following cardiorespiratory outcomes could be obtained:

- Doctor diagnosis of Asthma
- Wheezing
- Breathlessness
- Woken up by feeling of tight chest in the last 12 months
- Shortness of breath in the last 12 months
- Shortness of breath after exercise in the last 12 months
- Woken up by attack of shortness of breath in the last 12 months
- Phlegm from chest in winter
- Woken up by coughing in last 12 months
- Self-reported asthma
- Medication for asthma control
- Self-reported chest pain
- Self-reported hypertension
- Self-reported high cholesterol

An asthma symptom score was created from the responses to 8 asthma questions: wheezing in last 12 months, shortness of breath in last 12 months, woken up by feeling of tight chest in the last 12 months, attack of shortness of breath at rest in the last 12 months, attack of shortness of breath after exercise in the last 12 months, woken up by attack of breath in the last 12 months, self-reported asthma and medication for asthma control. A score of 1 was allocated for each positive response.

3.5 Exposure Characterisation

The annual average concentration of PM_{2.5} and NO₂ was estimated at each participant's address by land-use regression (LUR) models developed specifically for this study³⁹. In brief, the air pollution monitoring campaigns were performed during 2015-2016 in each study area. Weekly measurements of PM_{2.5} and NO₂ were performed in both winter and summer at 140 sites (40 sites each in three study areas, except 20 sites in Masiphumulele) within a period of 1 year. These measurements were temporally adjusted using routinely monitored air quality measurements to obtain the seasonal (winter/summer) and annual averages. Predictors of exposure, obtained or collected on-site, such as household density, nearby traffic (e.g. major roads, bus stops, and train stations), waste burning sites, and land-use derived from geographic information system (GIS) were used to evaluate the spatial variation in the annual average concentrations. To maximize the adjusted explained variance, regression models were developed, using a supervised stepwise approach, and the models were validated using leave-one-out-cross-validation (LOOCV). The LUR model was used to estimate annual average concentration of PM_{2.5} and NO₂ for each participant's address.

3.6 Statistical Analysis

A pilot study was conducted before the start of the main study to pilot the measuring instruments and logistics of the study.

Table 1 summarises the variables used in the data analysis.

Table 1: List of exposure and outcome variables

| Variable Name | Original Measurement scale | Units/Categorisation |
|---|-----------------------------------|---|
| Age | Numerical | Years |
| Gender | Categorical | Female/Male |
| Education | Categorical | Never attended school or only pre- school or primary school/Completed Highschool |
| Employed | Categorical | Yes/No |
| Home language | Caegorical | Isixhosa/Afrikaans, English or other |
| Current Residence | Categorical | Have lived elsewhere/Have never lived elsewhere before |
| Type of place of birth | Categorical | Farm/Village in rural area/Small town/Suburb of a city/Inner City |
| House Type | Categorical | Brick house/Shack/ Other (Room in back yard, shack in backyard, Hut, Caravan, Wood house |
| Air conditioning in home | Categorical | Yes/No |
| Fuel used to heat house or cooking | Categorical | Fuel other than electricity (wood, coal, gas, paraffin, cattle manure, solar or charcoal)/Electricity |

| | | |
|---|-------------|---|
| Door or window open while cooking | Categorical | Most of the time/Some of the time/Rarely/Do not have a door or window that opens to the outside |
| Sleep with open windows | Categorical | All of the time/Sometimes/Never |
| Water damage to building or its content | Categorical | Yes/No |
| Water damage in last 12 months | Categorical | Yes/No |
| Damp spots inside house in last 12 months | Categorical | Yes/No |
| Efforts done to reduce allergies | Categorical | Yes/No |
| Have Pets | Categorical | Yes/No |
| Frequency of walking a mile or more without stopping in the last month | Numerical | 1-100 |
| Exercise done in past month | Categorical | Yes/No |
| Number of times exercise per month | Numerical | 1-100 |
| Receiving Emotional Support | Categorical | Yes/No |
| Received emotional support within last 12 months | Categorical | Yes/No |
| Receiving financial support | Categorical | Yes/No |
| Smoke cigarettes | Categorical | Yes/No |
| Daily number of cigarettes smoked | Numerical | 1-100 |
| Number of years smoking | Numerical | 1-100 |
| Pack years | Numerical | 1-100 |
| Doctor diagnosed asthma | Categorical | Yes/No |
| Wheezing in the last 12 months | Categorical | Yes/No |
| Shortness of breath in last 12 months | Categorical | Yes/No |
| Woken up by feeling of tight chest in the last 12 months | Categorical | Yes/No |
| Attack of shortness of breath at rest in the last 12 months | Categorical | Yes/No |
| Attack of shortness of breath after exercise in the last 12 months | Categorical | Yes/No |

| | | |
|--|-------------|-------------------|
| Woken up by attack of shortness of breath in the last 12 months | Categorical | Yes/No |
| Bring up phlegm from chest at any time of day in the winter | Categorical | Yes/No |
| Woken up by heavy coughing at any time in the last 12 months | Categorical | Yes/No |
| Self-reported asthma | Categorical | Yes/No |
| Medication for asthma control | Categorical | Yes/No |
| Affected by animals, dust or pollen from trees or flowers | Categorical | Yes/No |
| Self-reported experience Chest Pain | Categorical | Yes/No |
| Self-reported hypertension | Categorical | Yes/No |
| Self-reported cholesterol | Categorical | Yes/No |
| NO₂ (summer) | Numerical | µg/m ³ |
| NO₂ (winter) | Numerical | µg/m ³ |
| NO₂ (annual) | Numerical | µg/m ³ |
| PM_{2.5} (summer) | Numerical | µg/m ³ |
| PM_{2.5} (winter) | Numerical | µg/m ³ |
| PM_{2.5} (annual) | Numerical | µg/m ³ |

Data was captured, cleaned and analysed in Stata: Release 11 (StataCorp. 2009. Statistical Software. College Station, TX: StataCorp LP). Descriptive statistics was used to examine the characteristics of the study population, cardiorespiratory outcomes and various confounders. Bivariate regression was used to measure associations between various confounders and cardio respiratory outcomes. Confounders identified apriori and those with significant associations ($p < 0.15$) were included in multi logistic regression models (Appendix D). Forward selection was then used to select the most parsimonious model. Collinearity of variables was assessed by calculating the variable inflation factor and variables with an inflation factor greater than 10 were removed from each model. Only variables described in literature to be associated with the outcomes variables and those with a biological plausible relation to the outcome variables were included in the models to .Area was not adjusted for in the models as it did not uncover any significant associations and did not improve the models in the sensitivity analysis.

3.7 Study Limitations

The study was restricted to the Western Province which could have different air pollution levels to other provinces. The findings of this study should therefore not be extrapolated to other provinces. Furthermore, the outcome measure was collected with questionnaires and so misclassification of outcomes could have occurred. Lastly, the cross-sectional nature of the study means that inferences about causality cannot be made.

3.8 Ethical Considerations

The larger study was done in accordance with the Declaration of Helsinki of the 25th world Medical Assembly. The main study was approved by the University of Cape Town's Research Ethics Committee (ethics number: 234/2009). The protocol for the sub study was approved by the University of Cape Town's Research Ethics Committee (ethics number: 639/2018).

The houses of school children from the main study was visited by trained field staff to explain the study, answer the questions that the parents/guardians had, obtain the caregivers (parent or guardians) consent and complete the European Community Respiratory Health Survey and National Health and Nutrition Examination Survey questionnaire. Informed consent from the caregivers was obtained. The consent form explained: the proposed research, risks and discomforts of testing, the expected benefits of the research, how confidentiality would be preserved and how confidentiality would be documented, there would be no costs for testing and list the details of people that could be contacted regarding the research. It also served as an assurance that participants could decline to participate in the study with no penalty.

All information and data are kept in records at the University of Cape Town. All files are locked in cabinets. To protect confidentiality, the consent forms and contact information sheets are stored apart from the confidential study information. They are kept in a separate locked file cabinet. Participants were referred to their local clinic or family practitioner for further management when problems were detected.

The findings of the research will be disseminated through journal publications as scientific literature. A copy of the report will also be made available at the University of Cape Town Medical School Library. Furthermore, information sheets on the risk of air pollution and how to manage these risks were distributed to school staff and caregivers of participating students.

4. Logistics

4.1 Work plan for 2018

[illegible]

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PART B : STRUCTURED LITERATURE REVIEW

1. Background

The World Health Organisation (WHO) has estimated that in 2016 4.2 million deaths were attributed to ambient air pollution. Furthermore, the majority of these deaths occurred in lower and middle-income countries with cardiorespiratory diseases being the main mechanism through which these deaths occurred¹.

Although the pollutant mix is complex, the WHO Air Quality Guidelines (AQG) identified four important criteria ambient air pollutants that have adverse health effects. These pollutants include: particulate matter (PM), sulphur dioxide (SO₂), nitrogen dioxide (NO₂) and ozone(O₃)². Additionally, carbon monoxide (CO) has also been shown to have adverse health effects³. Table 1 summarises the main properties of the air pollutants²⁻²².

Table 1: Summary air pollutants

| Air pollutant | Source | General information | Detrimental effects | Recommended Levels |
|----------------------------|---|--|---|---|
| Particulate Matter (PM) | Vehicle emissions, agriculture, power generation | <ul style="list-style-type: none"> -Most dangerous air pollutant -Components include: mineral dust, black carbon, ammonia, sodium chloride, sulphate nitrates and water -Commonly classified according to size: coarse ($PM_{2.5-10} \mu m$), fine ($PM \leq 2.5 \mu m$ or $PM_{2.5}$) and ultrafine ($PM < 0.1 \mu m$ or $PM_{0.1}$) | <ul style="list-style-type: none"> -Increases blood pressure by decreasing Nitrogen Dioxide (vasodilator) or increasing endothelin-1 (vasoconstrictor) -Induces oxidative stress and consequently, pulmonary and systemic inflammation -Puts the body in a pro coagulant state -Impairs mucociliary and macrophage activity and causes airway irritation -Prolonged exposure causes bronchial remodelling and it can be carcinogenic | <p><u>WHO Air Quality Guideline</u></p> <ul style="list-style-type: none"> -$PM_{2.5}$: $10 \mu g/m^3$ annual mean and $25 \mu g/m^3$ daily mean -PM_{10}: $20 \mu g/m^3$ annual mean and $50 \mu g/m^3$ daily mean <p><u>South African National Ambient Air Quality Standards (SA-NAAQS)</u></p> <ul style="list-style-type: none"> -$PM_{2.5}$: $20 \mu g/m^3$ annual mean and $40 \mu g/m^3$ daily mean -PM_{10}: $40 \mu g/m^3$ annual mean and $75 \mu g/m^3$ daily mean |
| Sulphur Dioxide (SO_2) | Fossil fuel combustion at power plants and other industrial facilities, extraction of metal ore, burning of high sulphur containing fuels by vehicles, large ships and non-road equipment | <ul style="list-style-type: none"> -Precursor to acid rain which results in deforestation | <ul style="list-style-type: none"> -Reduces cardiac vagal tone and increases susceptibility to arrhythmias -Irritant to eyes, nose, throat and respiratory tract | <p><u>WHO Air Quality Guideline</u></p> <ul style="list-style-type: none"> -$500 \mu g/m^3$ over 10-minute mean duration -$20 \mu g/m^3$ over 24 hours <p><u>South African National Ambient Air Quality Standards (SA-NAAQS)</u></p> |

| | | | | |
|------------------------------------|--|---|---|---|
| | | | - Causes cough and facilitates bronchoconstriction | -500 $\mu\text{g}/\text{m}^3$ over 10-minute mean duration -125 $\mu\text{g}/\text{m}^3$ over 24 hours |
| Nitrogen Dioxide (NO_2) | Combustion processes used in generating power, heating, ships and vehicles | -Plays a primary role in the formation of ozone | -Impairs gaseous exchange and increases myocardial stress -Increases bronchial reactivity and susceptibility to respiratory infections | <u>WHO Air Quality Guideline</u> -1-hour average of 200 $\mu\text{g}/\text{m}^3$ - 40 $\mu\text{g}/\text{m}^3$ annual average <u>South African National Ambient Air Quality Standards (SA-NAAQS)</u> -1 hour average of 200 $\mu\text{g}/\text{m}^3$ - annual average of 40 $\mu\text{g}/\text{m}^3$ |
| Ozone (O_3) | Troposphere | -Formed by photochemical reactions in the presence of precursor pollutants such as Nitrogen Oxides and Volatile Organic Compounds -Depicts seasonal and diurnal patterns with higher concentrations in summer and in the afternoon (due to its photochemical origin) | -Impairs gaseous exchange and increases myocardial stress -Induces Respiratory tract mucosal inflammation | <u>WHO Air Quality Guideline</u> -8-hour average of 100 $\mu\text{g}/\text{m}^3$ per day <u>South African National Ambient Air Quality Standards (SA-NAAQS)</u> -8-hour average of 120 $\mu\text{g}/\text{m}^3$ per day |

| | | | | |
|----------------------|--|--|---|---|
| Carbon Monoxide (CO) | Gas stoves, wood stoves, fireplaces and vehicles | | <p>-Reduces oxygen delivery to the body's organs</p> <p>Acute exposure has been associated with headache, dizziness on exertion, nausea and mental confusion</p> <p>-Chronic exposure has been associated with flu like symptoms, unconsciousness and death</p> | <p><u>Environmental Protection Agency Ambient Air Quality Standards</u></p> <p>-8-hour average of 9ppm</p> <p>-1-hour average of 35ppm</p> <p><u>South African National Ambient Air Quality Standards (SA-NAAQS)</u></p> <p>-8-hour average of 8.7ppm</p> <p>-1 hour average of 26ppm</p> |
|----------------------|--|--|---|---|

2. LITERATURE REVIEW

2.1 Objective of Literature Review

The literature review will summarise the findings of various epidemiological studies conducted internationally and in Africa investigating the relationship between air pollutants and various cardiorespiratory outcomes. The rationale is to determine the current state of evidence and identify gaps in the literature in terms of methodological approaches used to determine the association between ambient air pollution and cardiorespiratory outcomes in adults.

2.2 Search strategy

Selection criteria included peer-reviewed primary research articles aimed at exploring the association between ambient air pollution cardiorespiratory outcomes using epidemiological study designs. Subject-specific databases (such as Medline through PubMed; CINAHL; Highwire; and the Cochrane library) were searched using keywords combined by Boolean operators such as ‘**AND/ OR**’ commands. Keywords were identifying using the PICO (Population-Intervention-Comparison-Outcome) acronym and Medical Subject Headings (MeSH terms). The first stage of literature search was a broad search strategy with the query: ‘Ambient AND Air pollution AND Cardiovascular OR Respiratory AND Disease’. Furthermore, a second search with the following query was performed: ‘Ambient AND Air pollution AND Cardiovascular OR Respiratory AND Disease’. This was followed by a more specific search including all elements of the selection criteria and different MeSH terms to narrow-down the search with the query; ‘((Ambient air pollution OR Particulate Matter OR Sulphur dioxide OR Carbon monoxide OR Nitrogen dioxide) AND (Cardiovascular OR Respiratory) AND (Disease) AND Humans[Mesh]’. Furthermore, the reference lists of articles found during the electronic search were used to obtain more articles.

2.3 Ambient air pollution and cardiovascular disease

2.3.1 History of epidemiological association between ambient air pollution and cardiovascular disease

The association between air pollution and disease can be dated back to the early 20th century where winter episodes had been known to be associated with increased cardiovascular mortality^{23, 24}. Since then, a multitude of epidemiological studies have been published investigating this relationship.

2.3.2 Cardiovascular Health Outcomes of chronic ambient air pollution effects

The Harvard Six Cities study, a prospective cohort study involving 8111 adults, showed that the overall mortality rate ratio for adults living in the most polluted versus the least polluted city was 1.26 (95% CI 1.08 to 1.47). Furthermore, deaths attributed to cardiovascular causes accounted for the largest category of increased mortality²⁵. These results were reinforced by analysis of data from the ACS Cancer Prevention 2 study²⁶. A follow up of this study found that a 10µg/m³ increase in annual PM_{2.5} mean concentration was shown to be associated with a 6% increase in cardiopulmonary mortality²⁷. Similarly, in Seoul, a 10 µg/m³ increase in PM_{2.5} was found to be associated with a 1.36 (95%CI 1.11 to 1.66) increased risk of cardiovascular related deaths and an interquartile increase in SO₂ was found to be associated with 1.50(95%CI 1.14 to 1.96) increased risk of cardiovascular attributable deaths²⁸

Analysis of air pollutant exposure and blood pressure readings of adult Americans 57 years and older enrolled in the National Social Life, Health and Ageing project found that a 3.91µg/m³ increase in yearly PM_{2.5} was associated with a 1.24(95%CI 1.11 to 1.38) increase prevalence odds of hypertension²⁹. Similar findings were found in Taiwan where a 10µg/m³ increase in PM_{2.5} was found to be associated with a 0.45mmHg (95%CI 0.40 to 0.50), 0.07mmHg (95CI 0.04 to 0.11) and 0.38(95% CI 0.33 to 0.42) increase in systolic blood pressure, diastolic blood pressure and pulse pressure respectively. Furthermore, each 10µg/m³ increase in 2-year average PM_{2.5} was found to increase one's risk of developing hypertension by 3% (hazard ratio = 1.03, 95% CI 1.01 to 1.05)³⁰.

2.3.3 Cardiovascular Health Outcomes of acute ambient air pollution effects

The NMAPS study conducted in the United States of America found that a 10µg/m³ increase in PM₁₀ was associated with a 0.31% (95%CI 0.22% to 0.40%) increase in cardiopulmonary mortality³¹. This association was stronger in the APHEA-2 study where a 10µg/m³ increase in PM₁₀ was found to be associated with a 0.69% (95% CI 0.31% to 1.08%) increase in cardiovascular mortality³². Similar results were reported in various studies conducted across Asia: a study conducted in thirteen Japanese cities found that a 10µg/m³ increase in PM_{2.5} was associated with a 1.0091 (95% CI 1.0057 to 1.0125) increase in cardiovascular mortality³³; a multicity study involving four Chinese cities found that a 10µg/m³ increase in PM₁₀ was associated with a 0.58% (95%CI 0.22 to 0.93) excess risk of cardiovascular mortality³⁴ and studies conducted in Hong Kong and Beijing found that a 10µg/m³ increase in PM₁₀ and PM_{2.5} were associated with a 0.58%(95%CI 0.14% to 1.03%) and 0.39% (95%CI 0.21% to 0.59%) increase in cardiovascular related mortality respectively^{35,36}. Moreover, results from a time series study conducted in Shanghai showed that an increase of 10µg/m³ in PM₁₀, SO₂ and NO₂ corresponded to a 1.008(95%CI 1.000 to 1.016), 1.017(95%CI 0.998 to 1.036) and 1.029(95%CI 1.001 to 1.057) relative risk of stroke mortality respectively. However, in multipollutant models, the effects were weakened and were non-significant³⁷

As part of the APHEA project, a study conducted in Europe involving eight European cities found that a 10µg/m³ increase in PM₁₀ was associated with a 0.5% (95% CI 0.2% to 0.8%)

increase in hospital admissions attributed to cardiovascular causes ³⁸. Similarly studies conducted in China and Iran found that a $10\mu\text{g}/\text{m}^3$ increase in PM_{10} was associated with a 1.008(95%CI 0.997 to 1.020) and 1.007(95%CI 1.001 to 1.012) increase in risk of cardiovascular related hospital admissions and a $10\mu\text{g}/\text{m}^3$ increase NO_2 was associated with 1.014(95%CI 1.003 to 1.024) and 1.033(95% 1.010 to 1.055) increased risk of cardiovascular related hospital admissions ^{39,40}. Moreover, in Italy, a $10\mu\text{g}/\text{m}^3$ increase in PM_{10} and $\text{PM}_{2.5}$ were associated with a 1.4%(95CI 0.7% to 2.3%) and 3%(95%CI .47% to 4.7%) increase in emergency hospital visits due to atrial fibrillation respectively and in Beijing a $10\mu\text{g}/\text{m}^3$ increase in $\text{PM}_{2.5}$ was found to be associated with up to a 0.74%(95%CI 0.27% to 1.22%) increase in angina related hospital visits ^{41, 42}.

Air pollution has also been shown to influence self-reported morbidity. A study conducted in Eastern Estonia found that an interquartile increase in $\text{PM}_{2.5}$ was associated with a 1.13(95%CI 1.02 to 1.26) increased odds of self-reported chest pain ⁴³. In the United States of America, a $10\mu\text{g}/\text{m}^3$ increase in $\text{PM}_{2.5}$ was found to be associated with a 1.05(95%CI 1.00 to 1.10) and 1.08(95%CI 1.00 to 1.16) increased odds of self-reported hypertension and heart disease respectively⁴⁴. Conversely, a study conducted in Australia investigating the relationship between NO_2 and self-reported disease and symptoms found non-significant associations between increased levels of NO_2 and self-reported hypertension, stroke, heart disease, chest pain and palpitations ⁴⁵.

2.3.4 Ambient air pollution and cardiovascular disease in Africa

Ghana and South Africa were included in the World Health Organisation Study on Global Ageing and Adult Health. Analysis of data from the study found that there was a 1.13(95%CI 1.05 to 1.22) increased odds of stroke with each $10\mu\text{g}/\text{m}^3$ increase in $\text{PM}_{2.5}$ ⁴⁶. In addition, in South Africa, an interquartile ($12\mu\text{g}/\text{m}^3$) increase in PM_{10} was also found to be associated with a 4.1%(95%CI 0.4 to 8.1) increased risk of mortality attributed to cerebrovascular causes and a $12\text{mg}/\text{m}^3$ increase in NO_2 was found to be associated with a 3.4%(95%CI 0.3 to 6.6) and 8%(95%CI 2.9% to 13.4%) increased risk of mortality attributed to cardiovascular and cerebrovascular diseases respectively⁴⁷. Furthermore, in Algeria, it was found that decreasing PM_{10} annual mean by $5\mu\text{g}/\text{m}^3$ would avoid 3 cardiac hospitalisations ⁴⁸

2.4 Ambient air pollution and respiratory disease

2.4.1 Epidemiological association between ambient air pollution and respiratory disease

Various epidemiological studies have also demonstrated associations between the above-mentioned air pollutant and the respiratory system.²²

2.4.2 Ambient air pollution and lung function

The ESCAPE study, a multi-centre cohort study conducted amongst adult Europeans found that a $10\mu\text{g}/\text{m}^3$ increase in NO_2 exposure was associated with lower levels of FEV_1 and FVC: -14.0 mL (95%CI -25.8 to -2.1) and -14.9 mL (95% CI -28.7 to -1.1) respectively.

Furthermore, a $10\mu\text{g}/\text{m}^3$ increase in PM_{10} was also associated with lower levels of FEV_1 and FVC: -44.6mL (95%CI -85.4 to -3.8) and -59.0mL (95%CI -112.3 to -5.6)⁴⁹. A study investigating the relationship between exposure to chronic air pollution and adult lung function conducted by Forbes et al found that a $10\mu\text{g}/\text{m}^3$ increase in PM_{10} , NO_2 , SO_2 and O_3 were associated with a -92 mL (95%CI -129 to -55), -22 mL (95%CI -31 to -14), -22 mL (95%CI -36 to -7) and -4mL(95%CI, -26 to 19) change in FEV_1 respectively and in Switzerland, a $10\mu\text{g}/\text{m}^3$ increase in PM_{10} , NO_2 , SO_2 and O_3 was found to be associated with a -1.59 mL, -1.24 mL, -0.70 mL and 0.70 mL change in FEV_1 (P value: <0.001, <0.001, <0.001 and <0.01 respectively)^{50,51}. Similarly, in Korea, a $10\mu\text{g}/\text{m}^3$ increase in PM_{10} was found to be associated with a -0.39 L/min (95%CI, -0.63 to -0.14) change in PEFR ⁵².

Moreover, a crossover study conducted in London amongst adult asthmatics found that 2 hour exposure to a street with higher levels of particulate matter, elemental carbon and nitrogen dioxide reduced one's FEV_1 and FVC by 6.1% and 5.4% (p value 0.04 and 0.01) and a study investigating the association between traffic exposure and lung function found an inverse relationship between traffic density and lung function: relative to the lowest quartile of traffic density, the adjusted differences across increasing quartile were 5.1 mL(95%CI, -21.7 to 31.9), -15.4 mL (95%CI, -42.3 to 11.5) and -21.5 mL (95%CI, -48.5 to 5.5) for FEV_1 and 1.2 mL (95%CI, -30.4 to 32.7), -23.4 mL (95%CI, -55.0 to 8.2) and -34.8 mL (95%CI -66.5 to -3.1) for FVC respectively^{53,54}. Similarly, a study conducted in Tokyo among adult females found that after stratifying females into three groups according to traffic pollution exposure, the annual mean change in FEV_1 was greatest in group 1 (highest exposure to suspended particulate matter and nitrogen dioxide: -0.020L/year) and lowest in group 3 (lowest exposure to suspended particulate matter and nitrogen dioxide: -0.009L/year). Group 2 (second highest exposure to suspended particulate matter and nitrogen dioxide) had a -0.015L/year change in annual mean FEV_1 . The trend test thus showed that the higher the level of air pollution, the more significantly the FEV_1 was reduced (p <0.001)⁵⁵.

The inverse relationship between air pollution and lung function has also been depicted in children⁵⁶.

2.4.3 Ambient air pollution and asthma

A vast number of epidemiological studies have investigated the impact of ambient air pollution on asthma. A cross sectional study conducted in Taiwan amongst 32672 school children found that a 10ppb increase in O_3 was associated with a 1.138(95CI 1.001 to 1.293) odds of physician diagnosed asthma. Increasing levels of SO_2 and PM_{10} were however associated with decreased odds of physician diagnosed asthma and increasing levels of NO_2 was associated with a non-significant change in physician diagnosed asthma⁵⁷. Similarly, in Oslo Norway, an interquartile increase in NO_2 was associated with 0.81 (95CI 0.85 to 1.02) odds of asthma amongst 2871 children⁵⁸.

Conversely, a multitude of epidemiological studies have found significant associations between ambient air pollution and asthma. A cohort study conducted in Southern California amongst 3535 children found that the relative risk of developing asthma amongst children playing three or more sports was 3.3(95%CI 1.9 to 5.8) compared to children playing no sports⁵⁹. The PIAMA study conducted in the Netherlands found that an interquartile increase in PM_{2.5} was associated with a 1.26(95%CI 1.04 to 1.51) and 1.28(95%CI 1.10 to 1.49) increased odds of prevalent and incident asthma respectively⁶⁰. Analysis of the data from the Tasmanian Longitudinal Health Study found that participants who did not have asthma at the age of 45 and lived less than 200 meters from a major road were 5.32(95%CI 1.07 to 25.4) times as likely to have asthma that persisted from age 50 to 53 years compared to participants who lived more than 200 meters from a major road⁶¹.

2.4.4 Ambient air pollution and Chronic Obstructive Pulmonary Disease (COPD)

A cross sectional study conducted among adult females in Germany found the following: living less than 100 meters from a major road was associated with a 1.79(95%CI 1.06 to 3.02) odds of having COPD and an interquartile increase in NO₂ and PM₁₀ were associated with a 1.39(95%CI 1.20 to 1.63) and 1.37(95%CI 0.98 to 1.92) odds of having COPD respectively⁶². Similarly, in Denmark, an interquartile range increase in NO₂ was found to be associated with an 8%(95%CI 2 to 14) increased risk of developing COPD and in Korea, a 10µg/m³ increase in PM_{2.5} and NO₂ were found to be associated with a 1.14(95%CI 1.00 to 1.30) and 1.79(95%CI 1.02 to 3.13) odds of having COPD respectively^{63, 64}.

Several studies have demonstrated the association between ambient air pollution and COPD morbidity. Various studies conducted in Asia have assessed the relationship between ambient air pollution and COPD related hospital visits. In Beijing, an interquartile range increase in PM_{2.5} was found to be associated with a 2.38%(95%CI 2.22% to 2.53%) and 6.03%(95%CI 5.19% to 6.87%) increase in daily COPD related out- and inpatient visits respectively⁶⁵. Also related, another Beijing study found that a 10µg/m³ increase in PM_{2.5} and PM₁₀ was found to be associated with a 0.53%(95%CI 0.01 to 1.06) and 0.53%(95%CI 0.07% to 1.00%) increase in hospital admissions for acute exacerbation of COPD respectively⁶⁶. Furthermore, in Hong Kong, a 10µg/m³ increase in SO₂, NO₂, O₃, PM₁₀ and PM_{2.5} was found to be associated with a 1.007(95ci 1.001 to 1.014), 1.026(95%CI 1.022 to 1.031), 1.034(95%CI 1.030 to 1.040), 1.024(95%CI 1.021 to 1.028) and 1.031(95%CI 1.026 to 1.036) relative risk of hospital admissions for acute exacerbation of COPD⁶⁷. Similar positive associations were depicted in the U.S where a 10µg/m³ increase in PM₁₀ was found to be associated with a 1.47%(95% CI 0.93 to 2.01) increase in COPD related hospital admissions⁶⁸.

2.4.5 Ambient air pollution and Lung Cancer

A study conducted in Guangzhou China found that PM_{2.5} contributed to 23.1% of the lung cancer burden in 2013 and in Alberta PM_{2.5} contributed to between 1.87% and 5.69% of incident lung cancer cases⁶⁹. Several other studies have demonstrated associations between ambient air pollution and lung cancer⁷⁰.

In Korea, a 10µg/m³ increase in PM₁₀ and a 10ppb increase in NO₂ was found to be associated with a 1.09(95%CI 0.96 to 1.23) and 1.10(95%CI 1.00 to 1.22) odds of lung cancer incidence respectively⁷¹. Furthermore, analysis of data from the Adventist Health and Smog Study-2 found that a 10µg/m³ increase in PM_{2.5} was associated with a 1.43 (95%CI 1.11 to 1.84) risk of developing lung cancer⁷². Analysis of data from the Canadian National Breast Screening Study found that a 10µg/m³ increase in PM_{2.5} was found to be associated with a 1.34(95%CI 1.10 to 1.65) risk of developing lung cancer⁷³. These findings were reinforced by a meta-analysis conducted in China that found that a 10µg/m³ increase nitrogen

dioxide, nitrogen oxide, sulphur dioxide, and particulate matter was associated with a 1.06(95%CI 0.99 to 1.13), 1.04(95%CI 1.01 to 1.07), 1.03(95%CI 1.02 to 1.05) and 1.11(95%CI 1.00 to 1.22) odds of having lung cancer⁷⁴.

2.4.6 Ambient air Pollution and Lung Infection

Various experimental studies have demonstrated that air pollutants impair respiratory immunity and these findings have been subsequently confirmed by various epidemiological studies^{75, 76, 77}. A study conducted in Atlanta found that an interquartile increase in O₃ and NO₂ was associated with a 1.083(95%CI 1.038 to 1.131) and 1.025(95%CI 1.003 to 1.047) relative risk of being hospitalised for pneumonia amongst children between the ages of 0 and 4. Furthermore, an interquartile range increase in these pollutants were associated with a 1.041(95%CI 1.019 to 1.064) and 1.027(95%CI 1.016 to 1.039) relative risk of being hospitalised for upper respiratory tract infections⁷⁸. In Vietnam, an interquartile increase in NO₂ was found to be associated with 6.1%(95%CI 2.5% to 9.8%) increase in pneumonia hospital admissions amongst children between 0 and 17⁷⁹. These findings have been reinforced by systematic reviews and meta-analysis that found that a 10µg/m³ in PM_{2.5} and PM₁₀ were associated with a 1.8%(95%CI 0.5% to 3.1%) and 1.5%(95%CI 0.6% to 2.4%) excess risk of pneumonia hospitalisation respectively and a 10ppb increase in SO₂, O₃, and NO₂ were found to be associated with a 2.9%(95% CI 0.4% to 5.3%), 1.7%(95% CI 0.5% to 2.8%) and 1.4%(95%CI 0.4% to 2.4%) excess risk of pneumonia hospitalisation respectively⁸⁰.

Studies depicting associations between air pollution and respiratory infections have also been conducted in adults. A case crossover study conducted in Utah found that an interquartile increase in PM_{2.5} was associated with a 1.35(95%CI 1.06 to 1.80) odds of having pneumonia and in Rome, a 10µg/m³ increase in PM_{2.5} was found to be associated with a 2.8%(95%CI 0.5% to 5.2%) increased risk of lower respiratory tract hospitalisation^{81, 82}.

2.4.7 Ambient air Pollution and Respiratory Symptoms

In Eastern Estonia, an interquartile range increase in PM_{2.5} was found to be associated with a 1.16(95%CI 1.03 to 1.31) and 1.33(95%CI 1.04 to 1.42) increased odds of self-reported shortness of breath and asthma attack respectively⁴³. Furthermore, the RUPIOH study conducted in Europe amongst participants with asthma and COPD found that a 10µg/m³ increase in PM₁₀ was found to be associated with a 1.037(95%CI 1.002 to 1.074) and 1.027(95%CI 1.000 to 1.055) increased odds of self-reported shortness of breath and wheezing respectively⁸³. Analysis of data from the SAPALDIA study found that amongst participants who had never smoked, a 10µg/m³ increase in PM₁₀ was found to be associated with a 1.35(95%CI 1.11 to 1.65), 1.27(95%CI 1.08 to 1.50), 1.48(95%CI 1.23 to 1.78), 1.33(95%CI 1.14 to 1.55) and 1.32(95%CI 1.18 to 1.46) increased odds of chronic phlegm production, chronic cough or phlegm production, breathlessness during the day, breathlessness during the day or night and dyspnoea on exertion respectively and a study conducted in the Netherlands found that a 9.3 µg/m³ increase in soot and 17.6µg/m³ increase in NO₂ was associated with a 5.3(95%CI 1.2 to 23) and 3.8(95%CI 1.0 to 14) prevalence ratio of reporting phlegm^{84, 85}.

2.4.8 Ambient air pollution and respiratory disease in Africa

In South Africa, a 12mg/m^3 increase in PM_{10} and 12mg/m^3 increase in NO_2 were found to be associated with a 1.3% (95 CI, -1.4 to 4.0) and 2% (95%CI -1.6 to 5.7) increase in mortality attributable to respiratory diseases and cross sectional study conducted in Nigeria found a negative correlation between increasing levels of PM_{10} and lung function^{47, 86}. Furthermore, in Algeria, decreasing the annual PM_{10} by $5\mu\text{g/m}^3$ reduced five hospitable admissions attributable to respiratory diseases and a study conducted in Namibia also found a significant association between particulate matter and episodes of coughing and phlegm^{48,87}.

2.4.9 Review of studies investigating the relationship between ambient air pollution and cardiorespiratory disease in adults

Table 2 summarises the findings 13 systematic reviews investigating the relationship between ambient air pollution and cardiorespiratory disease in adults.

Table 2: Summary of systematic reviews investigating the relationship between ambient air pollutants and cardiorespiratory outcomes amongst adults ⁸⁸⁻⁹⁵

| Author | Title | Number of studies included | Review Period | Study Population | Results | Study Limitations |
|--|---|----------------------------|--------------------------------|---|---|--|
| Newell K, Kartsonaki C, Lam KBH, Kurmi O | Cardiorespiratory health effects of gaseous ambient air pollution exposure in low- and middle-income countries: a systematic review and meta-analysis | 60 studies | Studies from inception to 2016 | Studies were included if they examined the cardiorespiratory effects of gaseous AAP (NO _x , SO ₂ , O ₃ and CO) in adults and were performed within LMICs | <p>% excess relative risk <u>NO_x</u></p> <ul style="list-style-type: none"> • COPD mortality – (1.11 – 2.51) • COPD morbidity – 2.48 (1.49 – 3.46) • Heart disease mortality – 1.52 (0.98 – 2.06) • Heart disease morbidity - 1.08 (0.73 – 1.43) • Stroke mortality – 1.01 (0.79 – 1.24) • Stroke morbidity – 0.95 (0.64 – 1.26) | <ul style="list-style-type: none"> • Significant heterogeneity of pooled estimates • Included studies made use of fixed site monitoring as an estimate of individual exposure to air pollutants • Only studies published in English were included • No studies conducted in Africa were included |

| | | | | | | |
|--|--|--|--|--|---|--|
| | | | | | <ul style="list-style-type: none"> • Respiratory mortality – 0.86 (0.3 – 1.38) • Respiratory morbidity – 0.91 (0.34 – 1.49) SO ₂ <ul style="list-style-type: none"> • COPD mortality - 1.68 (0.71 – 2.64) • Heart disease mortality 1.31 (0.82 – 1.81) • Heart disease morbidity 0.36 (0.19 – 0.54) • Stroke mortality 0.64 (0.53 – 0.76) • Stroke morbidity - 0.23 (-0.06 – 0.51) • Respiratory morbidity – 1.64 (0.87 – 2.40) O ₃ | |
|--|--|--|--|--|---|--|

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|---|--|------------|-------------------------------|---|--|---|
| | | | | | <ul style="list-style-type: none"> Cardiovascular mortality - - 0.01 (-0.33 – 0.30) | |
| Song X, Liu Y, Hu Y, Zhao X, Tian J, Ding G, Wang S | Short – Term Exposure to Air Pollution and Cardiac Arrhythmia: A Meta – Analysis and Systematic Review | 25 studies | Studies from inception - 2015 | Case-crossover and time-series studies were included if they evaluated the short-term (up to seven days) association between air pollutants (gaseous pollutants: carbon monoxide, nitrogen dioxide, sulfur dioxide, or ozone; particulate components: PM _{2.5} or PM ₁₀) and arrhythmia hospitalization or mortality | <p>Relative risk associated with a 10 µg/m³ increase in PM_{2.5} and PM₁₀, 1ppm increase in CO and 10ppb increase in O₃,NO₂ and SO₂</p> <p>Hospitalisation</p> <ul style="list-style-type: none"> PM_{2.5} – 1.018 (1.005 – 1.025) PM₁₀ – 1.010 (1.004 – 1.015) CO – 1.060 (1.017 – 1.065) O₃ – 1.019 (0.997 – 1.035) NO₂ – 1.037 (1.018 – 1.055) SO₂ – 1.018 (1.000 – 1.040) | <ul style="list-style-type: none"> Significant heterogeneity of pooled estimates Included studies made use of fixed site monitoring as an estimate of individual exposure to air pollutants No studies conducted in Africa were included |

| | | | | | | |
|--|--|------------|-------------|---|--|--|
| | | | | | Mortality <ul style="list-style-type: none"> • PM_{2.5} – 1.027 (0.987 – 1.068) • PM₁₀ – 1.009 (0.994 – 1.024) • CO – 1.077 (0.790 – 1.467) • O₃ – 0.997 (0.975 – 1.018) • NO₂ – 1.026 (1.003 – 1.050) • SO₂ – 1.028 (0.988 – 1.069) | |
| Xialoe L, Hui L, Yanping R, Ruijuan L, Xiaogi Z, Michael R, Zhongjie F | Association of Exposure to Particular Matter and Carotid Intima – Media Thickness: A Systematic Review and Meta - Analysis | 13 studies | 1948 - 2015 | population-based studies, which not only reported the association between particular matter (PM _{2.5} or PM ₁₀) and CIMT, but also provided original data for particular matter (PM _{2.5} or PM ₁₀) | 10 µg/m ³ increase in PM _{2.5} and PM ₁₀ was found to be associated with a 16.79 µm (95% CI, 4.95–28.63 µm) and 4.13 µm (95% CI, –5.79–14.04 µm) increase in carotid intima media thickness. | <ul style="list-style-type: none"> • Significant heterogeneity of results • Included studies made use of fixed site monitoring as an estimate of individual exposure to air pollutants |

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|--------------------------------------|--|-------------|-----------|--|---|--|
| | | | | and carotid artery intima-media thickness | | <ul style="list-style-type: none"> • Only single pollutant effects assessed • No studies conducted in Africa were included |
| Shah AS, Lee KK, McAllister DA et al | Short term exposure to air pollution and stroke: systematic review and meta analysis | 103 studies | 1948-2014 | Studies investigating the short term associations (up to a lag of seven days) between carbon monoxide, sulphur dioxide, nitrogen dioxide, ozone, and particulate matter PM _{2.5} (fine particles <2.5 µm in size) or PM ₁₀ (coarse particles <10 µm in size) and admission to hospital for stroke or | Relative risk associated with incremental increase in air pollutant <ul style="list-style-type: none"> • CO (1ppm) : 1.015 (1.004 – 1.026) • SO₂ (10ppb) : 1.019 (1.011 – 1.027) • NO₂ (10 ppb) : 1.014 (1.009 – 1.019) • O₃ (10 ppb) : 1.001 (1.000 - 1.002) • PM_{2.5} (10 µg/m³) : 1.011 (1.011 – 1.012) • PM₁₀ (10 µg/m³) : | <ul style="list-style-type: none"> • Significant heterogeneity of results • Included studies made use of fixed site monitoring as an estimate of individual exposure to air pollutants • Only single pollutant effects assessed |

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| | | | | mortality from stroke | 1.003 (1.002 – 1.004) | |
| Shah AS, Langrish JP, Nair H et al | Global association of air pollution and heart failure: a systematic review and meta analysis | 35 studies | 1948-2012 | Peer reviewed original articles investigating the relationship between, carbon monoxide, sulphur dioxide, nitrogen dioxide, ozone, particulate matter and reported heart failure hospitalisation or heart failure mortality | % risk of heart failure hospitalisation or mortality associated with incremental increase in air pollutants <ul style="list-style-type: none"> • CO (1 ppm) : 3.52 (2.52 – 4.54) • SO₂ (10 ppb) : 2.36 (1.35 – 3.38) • NO₂ (10 ppb) : 1.70 (1.25 – 2.36) • O₃ (10 ppb) : 0.46 (-0.10 – 1.02) • PM_{2.5} (10 µg/m³) : 2.12 (1.42 – 2.82) • PM₁₀ (10 µg/m³) : 1.63 (1.20 – 2.07) | <ul style="list-style-type: none"> • Significant heterogeneity of pooled estimates • Only single pollutant effects assessed • No studies conducted in Africa were included |
| Orellano P, Quaranta N, Reynoso J, Balbi B, Vasquez J | Effect of outdoor air pollution on asthma exacerbation in children and adults: | 22 studies | 2000 - 2016 | Studies exploring the relationship between outdoor air pollution and acute | Odds of asthma exacerbation with an incremental increase air pollutant | <ul style="list-style-type: none"> • Significant heterogeneity of pooled estimates • Only single pollutant |

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|---------------------------|--|------------|-------------|---|---|---|
| | Systematic review and multilevel meta analysis | | | exacerbations of asthma in children and adults through a case-crossover observational design. | <ul style="list-style-type: none"> • SO₂ (10ppb) : 1.039 (0.988 – 1.094) • PM₁₀ (10 µg/m³) : 1.024 (0.995 – 1.053) • NO₂ (10ppb) : 1.024 (1.005 – 1.043) • PM_{2.5} (10 µg/m³) : 1.028 (1.009 – 1.047) • CO (1ppm) : 1.045 (1.005 – 1.086) • O₃ (1 ppb) 1.032 (1.005 – 1.060) | <p>effects assessed</p> <ul style="list-style-type: none"> • Study findings cannot be extrapolated to lower income countries • No studies conducted in Africa were included |
| Li J, Sun S, Tang R et al | Major air pollutants and risk of COPD exacerbations: a systematic review and meta analysis | 59 studies | 1946 - 2016 | Studies investigating the association between major air pollutants and COPD exacerbation | <p>Relative risk associated with incremental increase in air pollutant</p> <ul style="list-style-type: none"> • CO (100 µg/m³) : 1.01 (1.00 – 1.01) • SO₂ (10 µg/m³) : 1.01 (1.00 – 1.01) | <ul style="list-style-type: none"> • Only single pollutant effects assessed • No studies conducted in Africa were included |

| | | | | | | |
|--|--|------------|-------------|--|---|--|
| | | | | | <ul style="list-style-type: none"> • NO₂ (10 µg/m³) : 1.04 (1.03 – 1.06) • O₃ (10 µg/m³) : 1.01 – 1.04) • PM_{2.5} (10 µg/m³) : 1.02 (1.01 – 1.04) • PM₁₀ (10 µg/m³) : 1.02 (1.01 – 1.02) | |
| Moore E, Chatzidiakou L, Kuku MO et al | Global Associations between Air Pollutants and Chronic Obstructive Pulmonary Disease Hospitalizations. A Systematic Review | 46 studies | 1980 - 2015 | Time series and case cross over studies assessing the effects of air pollution on COPD | <p>Odds of COPD hospitalisation associated with incremental increase in air pollutant</p> <ul style="list-style-type: none"> • PM₁₀ (10 µg/m³) : 1.01 (1.00 – 1.01) • O₃(10 µg/m³) : 1.02 (1.01 – 1.03) • SO₂ (10 µg/m³) : 1.00 (1.00 – 1.01) • PM_{2.5} (10 µg/m³) : 1.03 (1.01 – 1.05) • CO (mg/m³) : 1.02 (1.01 – 1.03) | <ul style="list-style-type: none"> • Significant heterogeneity of pooled estimates • Only single pollutant effects assessed • Included studies made use of fixed site monitoring as an estimate of individual exposure to air pollutants • No studies conducted in |

| | | | | | | |
|--|--|--|--|--|---|-------------------------|
| | | | | | <ul style="list-style-type: none"> NO₂ (10 μg/m³) : 1.03 (1.02 – 1.05) | Africa were included |
|--|--|--|--|--|---|-------------------------|

3. Conclusion

The majority of epidemiological studies investigating the relationship between ambient air pollution and cardiorespiratory outcomes were conducted in America, Asia and Europe despite the majority of ambient air pollution related deaths occurring in lower- and middle-income countries. Levels of air pollution and air pollutant composition on these continents differ from those found in Africa. Furthermore, the burden of disease in developed countries differs from those in developing countries and so various confounding factors present in developed countries and absent in developing countries could contribute to the above demonstrated associations. Moreover, majority of the studies made use of fixed site monitoring to assess each individual's exposure to the various air pollutants and the interactive effects of pollutants on health were not investigated as evidenced by the reporting of results for single pollutant models. Multiple outcomes were also assessed in these studies. A common limitation in the African studies investigating the relationship between ambient air pollution and cardiovascular outcomes is the lack of accurate measurements representing each participant's true exposure to the above-mentioned air pollutants and so the observed associations may not represent true associations between air pollution and cardiorespiratory outcomes. Therefore, in the African context, further studies with more accurate exposure measurements should be conducted to contribute to the paucity of evidence available regarding the relationship between air pollution and cardiorespiratory outcomes.

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Ambient air pollution and cardiorespiratory outcomes amongst adults residing in four informal settlements in the Western Province of South Africa

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ABSTRACT

Background

Many studies investigating the relationship between ambient air pollution and cardiorespiratory outcomes have been conducted in developed countries despite more vulnerable populations in low- and middle-income countries especially in Africa. No studies previous studies have been done in South Africa informal settlements.

Aim

The aim of the study was to investigate the relationship between ambient air pollutant exposure and self-reported cardiorespiratory outcomes amongst adults residing in four informal settlements of the Western Province of South Africa.

Methods

This cross-sectional study included 572 adults from four informal settlements (Khayelitsha, Marconi Beam, Oudtshoorn and Masiphumele) in the Western Cape, South Africa. The study made use of Land Use Regression to estimate each participant's exposure to particulate matter of aerodynamic diameter of $2.5\mu\text{m}$ ($\text{PM}_{2.5}$) and nitrogen dioxide (NO_2). A questionnaire was adapted from the European Community Respiratory Health Survey and National Health and Nutrition Examination Survey questionnaire to collect data on self-reported cardiorespiratory outcomes and specific confounding factors of interest.

Results

The median age the participants was 39 years (Interquartile Range (IQR): 33 - 45) with 88.5% female. The median NO_2 level was $22.4\text{ }\mu\text{g}/\text{m}^3$ (IQR: 13.3 – 24.1) and the median $\text{PM}_{2.5}$ level was $10.6\text{ }\mu\text{g}/\text{m}^3$ (IQR: 8.7 – 13.1). An increase of $10\mu\text{g}/\text{m}^3$ in annual NO_2 level was found to be associated with a 2.9 (95%CI: 1.3 to 6.1) odds of having self-reported chest pain, adjusting for $\text{PM}_{2.5}$ and confounders. No other significant association was found indicating an adverse health effect due to air pollution.

Conclusion

The study found preliminary circumstantial evidence of an association between annual ambient NO_2 exposure and self-reported chest pain (a crude proxy of angina related pain), even at levels below both WHO Air Quality Guidelines and the South African National Ambient Air Quality Standards. However, the results should be interpreted cautiously due to the self-reported nature of the outcome measure and the cross-sectional design of the study.

1. Introduction

In 2016, the World Health Organisation estimated that 4.2 million deaths were attributed to ambient air pollution¹. The majority of deaths attributable to cardiovascular and respiratory disease¹ were particulate matter (PM), sulphur dioxide (SO₂), nitrogen dioxide (NO₂) and ozone (O₃)² and carbon monoxide (CO).

Despite the majority of ambient air pollution related deaths occurring in low and middle income countries, most studies investigating the relationship between ambient air pollution and cardiorespiratory outcomes have been conducted in developed countries where air pollution levels and composition as well as population characteristics differ from those in Africa and more specifically in South Africa's informal settlements^{1,4-11}. Furthermore, epidemiological studies conducted in Africa investigating this relationship have notable limitations including a lack of robust exposure measurements, lack of objective outcome measurements and inadequate adjustment of possible confounders¹²⁻¹⁶.

There is therefore a paucity of robust data on the continent describing the relationship between ambient air pollution and cardiorespiratory outcomes, especially amongst adults residing in informal settlements. This study aimed to determine the relationship between PM_{2.5} and NO₂ exposure estimated using land use regression analysis and self-reported cardiorespiratory outcomes amongst adults residing in four informal settlements of the Western Province of South Africa.

2. Methods and Materials

2.1 Study design, population and sampling

This study involved the analysis of a sub-set of data that was collected as part of a larger study conducted during 2015-2016 and investigating the effect of ambient air pollution on asthma among 590 primary school pupils in the Western Cape¹⁷. This sub-study used the cross-sectional data from the baseline study conducted in 2015 investigating the association between ambient air pollution and cardiorespiratory outcomes among the caregivers of the child participants. The study areas included informal settlements in three areas prioritised in a needs analysis conducted by the department of Environmental Affairs and Development Planning (DEADP) in 2013. These areas included an urban industrialised area (Marconi Beam in Milnerton), a peri-urban area with a large informal sector (Khayelitsha) and a semi arid rural area (Oudtshoorn). An additional area (with a low air pollution score ranking) with comparable socio-economic status as the three identified areas was included (Mashipumelele in Noordhoek). These areas were selected to maximise contrasts in exposure levels to the different ambient air pollutants.

The sampling of child participants are detailed elsewhere¹⁷. Briefly, a list of all the schools in the study area was obtained from the Department of Education and access to one or two schools per area was established. Approximately 150 students in each study area was selected.

After meeting each school's principal, obtaining permission from the school board and obtaining class lists and addresses, the houses of school children were visited by trained field staff to obtain the caregivers (parent or guardian) consent. Only those who consented were included in the study. The caregiver of these children who was at home at the time of the survey were selected for this study.

2.2 Questionnaire

Trained interviewers administered the questionnaires to participants in their spoken language (English, Xhosa or Afrikaans). The principle investigator and study co-ordinator provided training on administration of the questionnaire to the fieldworkers. The questionnaire was back-translated to ensure the consistency and reliability of the questionnaires. The use of mobile technology was implemented in the administration and capture of questionnaires.

The questionnaire used for this study included items on: demographic characteristics, residential history, respiratory health, cardiovascular disease, blood pressure and other chronic illnesses such as high cholesterol, occupational history, exposure to indoor pollutants, exposure to outdoor pollutants, physical activity, psychosocial stress and tobacco use.

The European Community Respiratory Health Survey¹⁸ and National Health and Nutrition Examination Survey questionnaire¹⁹ was incorporated into the study's questionnaire. From these questionnaires the following cardio respiratory outcomes could be obtained: doctor diagnosis of asthma, wheezing in the last 12 months, shortness of breath in the last 12 months, woken up by feeling of tight chest in the last 12 months, attack of shortness of breath at rest in the last 12 months, attack shortness of breath after exercise in the last 12 months, woken up by attack of shortness of breath in the last 12 months, bring up phlegm from chest at any time of day in the winter, woken up by heavy coughing at any time in the last 12 months, self-reported asthma, medication for asthma control, self-reported chest pain, self-reported hypertension and self-reported high cholesterol. An asthma symptom score was created from the responses to 8 asthma questions: wheezing in last 12 months, shortness of breath in last 12 months, woken up by feeling of tight chest in the last 12 months, attack of shortness of breath at rest in the last 12 months, attack of shortness of breath after exercise in the last 12 months, woken up by attack of breath in the last 12 months, self-reported asthma and medication for asthma control. A score of 1 was allocated for each positive response.

2.3 Exposure Characterisation

The annual average concentration of PM_{2.5} and NO₂ was estimated at each participant's address by land-use regression (LUR) models developed specifically for this study²². In brief, the air pollution monitoring campaigns were performed during 2015-2016 in each study area. Weekly measurements of PM_{2.5} and NO₂ were performed in both winter and summer at 140 sites (40 sites each in three study areas, and 20 sites in Masiphumulele) within a period of 1 year. These measurements were temporally adjusted using routinely monitored air quality measurements to obtain the seasonal (winter/summer) and annual averages. Predictors of exposure, obtained or collected on-site, such as household density, nearby traffic (e.g. major roads, bus stops, and train stations), waste burning sites, and land-use derived from geographic information system (GIS) were used to evaluate the spatial variation in the annual average concentrations. To maximize the adjusted explained variance, regression models were developed, using a supervised stepwise approach, and the models were validated using leave-one-out-cross-validation (LOOCV). The LUR model was used to estimate annual average concentration of PM_{2.5} and NO₂ for each participant's address

2.4 Statistical Analysis

Data was captured, cleaned and analysed in Stata: Release 11 (StataCorp. 2009. Statistical Software. College Station, TX: StataCorp LP). Descriptive statistics was used to examine the characteristics of the study population, cardiorespiratory outcomes and various confounders. Bivariate regression was used to measure associations between various confounders and cardio respiratory outcomes. Confounders identified apriori and those with significant associations (p<0.15) were included in multi logistic regression models (Appendix D). Forward selection was then used to select the most parsimonious model. Collinearity of variables was assessed

by calculating the variable inflation factor and variables with an inflation factor greater than 10 were removed from each model. Only variables described in literature to be associated with the outcome's variables and those with a biological plausible relation to the outcome variables were included in the models. Area was not adjusted for in the models as it did not improve the models in the sensitivity analysis.

2.5 Ethical Considerations

The main study was done in accordance with the Declaration of Helsinki of the 25th world Medical Assembly. The main study was approved by the University of Cape Town's Research Ethics Committee (ethics number: 234/2009). The protocol for the sub study was approved by the University of Cape Town's Research Ethics Committee (ethics number: 639/2018).

3. Results

3.1 Demographic characteristics of the study participants

Table 1 shows that most participants were female (93.0%) and that Mashipumelele had the highest proportion of participants who had completed high school and were employed (86.6% and 51.8% respectively). The participants from Mashipumelele were also younger (median age 36) than the participants from Khayelitsha (median age 39), Oudtshoorn (median age 41) and Marconi Beam (median age 37). isiXhosa was the predominant home language spoken amongst participants from Khayelitsha (87.2%), Marconi Beam (84.8%) and Mashipumelele (97.3%) but not Oudtshoorn (20.5%). Villages in rural areas were the predominant place of birth of the participants (44.2%) and Mashipumelele's proportion of participants born in villages in rural areas (73.2%) was higher than Khayelitsha's (50.0%) Oudtshoorn's (1.9%) and Marconi Beam's (62.1%). Most of the participants had never resided elsewhere before (77.6%).

Table 1 Demographics and characteristics of the study participants

| | Khayelitsha (N = 172) n (%) | Oudtshoorn (N = 156) n (%) | Marconi Beam (N = 132) n (%) | Mashipumelele (N = 112) n (%) | All areas (N = 572) n (%) |
|---|--|---|---|--|--|
| Age (years) | 39 (33; 45) | 41 (34; 49) | 37 (31; 41) | 36 (32; 43) | 39 (33; 45) |
| Gender (female) | 160 (93.0) | 142 (91.0) | 121 (91.7) | 92 (82.14) | 515 (90.0) |
| Education | | | | | |
| Never attended school or only pre- school or primary school | 35 (20.3) | 45 (28.8) | 24 (18.2) | 15 (13.4) | 119 (20.8) |
| Completed High school | 137 (79.7) | 111 (71.2) | 108 (81.8) | 97 (86.6) | 453 (79.2) |
| Employed | 78 (45.3) | 50 (32.1) | 59 (44.7) | 58 (51.8) | 245 (42.8) |

| | | | | | |
|-----------------------------|------------|------------|------------|------------|------------|
| Home language | | | | | |
| Isixhosa | 150 (87.2) | 32 (20.5) | 112 (84.8) | 109 (97.3) | 403 (70.5) |
| Afrikaans, English or other | 22 (12.8) | 124 (79.5) | 20 (15.2) | 3 (2.7) | 169 (29.6) |
| Current Residence | | | | | |
| Have lived elsewhere | 47 (27.3) | 23 (14.7) | 29 (22.0) | 29 (25.9) | 128 (22.4) |
| Type of place of birth | | | | | |
| Farm | 10 (5.8) | 24 (15.4) | 4 (3.0) | 0 (0) | 38 (6.6) |
| Village in rural area | 86 (50.0) | 3 (1.9) | 82 (62.1) | 82 (73.2) | 253 (44.2) |
| Small town | 20 (11.6) | 8 (62.8) | 14 (10.6) | 15 (13.4) | 147 (25.7) |
| Suburb of a city | 9 (5.2) | 0 (0) | 5 (3.8) | 1 (0.9) | 15 (2.6) |
| Inner city | 47 (27.3) | 31 (19.9) | 27 (20.5) | 14 (12.5) | 119 (20.8) |

Categorical variables depicted as number (%)

Numerical variables depicted as median (25th percentile, 75th percentile)

3.2 Household characteristics of the study participants

Oudtshoorn had the highest proportion of participants who resided in brick houses (88.5%) compared to Khayelitsha (49.4%), Marconi Beam (54.6%) and Mashipumelele (21.4%). The prevalence of air conditioning use was less than 5 percent across the study areas and none of the participants from Oudtshoorn had air conditioners in their homes. Although electricity was the predominant source of energy used across the study areas (97.2%), almost half (49.0%) of the participants also made use of paraffin for cooking and heating. Almost a third (31.1%) of the participants from Marconi Beam did not have a door or window that opened to the outside. Khayelitsha had the highest proportion of participants who experienced water damage to their homes (22.1%) and the highest prevalence (16.9%) of participants who had intervened to reduce allergens in their homes. Participants residing in Oudtshoorn reported the highest proportion of pet ownership (44.9%).

Table 2: Household characteristics of the study participants

| | Khayelitsha (N = 172) n (%) | Oudtshoorn (N = 156) n (%) | Marconi Beam (N = 132) n (%) | Mashipumelele (N = 112) n (%) | All areas (N = 572) n (%) |
|---|--|---|---|--|--|
| House Type | | | | | |
| • Brick House | 85 (49.4) | 138 (88.5) | 72 (54.6) | 24 (21.4) | 319 (55.8) |
| • Shack | 69 (40.1) | 6 (3.9) | 14 (10.6) | 33 (29.5) | 122 (21.3) |
| • Other(Room in back yard, shack in backyard, Hut, Caravan, Wood house) | 18 (10.5) | 12 (7.7) | 46 (34.9) | 55 (49.1) | 131 (22.9) |
| Air conditioning in home | 6 (3.5) | 0 (0) | 3 (2.3) | 10 (8.9) | 19 (3.3) |
| Fuel used to heat house or cooking | | | | | |
| • Wood | 4 (2.3) | 6 (3.9) | 0 (0) | 0 (0) | 10 (1.8) |
| • Coal | 0 (0) | 0 (0) | 0 (0) | 1 (0.9) | 1 (0.2) |
| • Gas | 28 (16.3) | 16 (10.3) | 4 (3.0) | 4 (3.6) | 52 (9.1) |
| • Paraffin | 128 (74.4) | 3 (1.9) | 88 (66.7) | 61 (54.5) | 280 (49.0) |
| • Animal Dung | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) |
| • Solar energy | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) |

| | | | | | |
|--|------------|------------|------------|------------|------------|
| • Electricity | 166 (96.5) | 149 (95.5) | 131 (99.2) | 110 (98.2) | 556 (97.2) |
| Door or window open while cooking | | | | | |
| Most of the time | 42 (24.4) | 75 (48.1) | 6 (4.6) | 5 (4.5) | 121 (21.2) |
| Some of the time | 91 (52.9) | 88 (56.4) | 58 (43.9) | 64 (57.1) | 301 (52.6) |
| Rarely (or only occasionally) | 22 (12.8) | 0 (0) | 27 (20.5) | 29 (25.9) | 78 (13.6) |
| Do not have a door or window that opens to the outside | 17 (9.9) | 0 (0) | 41 (31.1) | 14 (12.5) | 72 (12.6) |
| Sleep with open windows | | | | | |
| All of the time | 31 (18.0) | 60 (38.5) | 22 (16.7) | 41 (36.6) | 154 (26.9) |
| Sometimes | 141 (83.0) | 96 (61.5) | 110 (83.3) | 71 (63.4) | 418 (73.1) |
| Water damage to building or its content | 38 (22.1) | 3 (1.9) | 19 (14.4) | 14 (12.5) | 74 (12.9) |
| Water damage in last 12 months | 32 (18.6) | 2 (1.3) | 17 (12.9) | 8 (7.1) | 59 (10.3) |
| Damp spots inside house in last 12 months | 57 (33.1) | 3 (1.9) | 15 (11.4) | 16 (14.3) | 91 (15.9) |

| | | | | | |
|----------------------------------|-----------|-----------|-----------|-----------|------------|
| Efforts done to reduce allergies | | | | | |
| Remove carpets, | 29 (16.9) | 2 (1.3) | 8 (6.1) | 5 (4.5) | 44 (7.7) |
| Bought a new carpet, | | | | | |
| Use anti dust mite sprays, | | | | | |
| Got rid of pets | | | | | |
| Have Pets | 38 (22.1) | 70 (44.9) | 15 (11.4) | 18 (16.1) | 141 (24.7) |

Categorical variables depicted as number (%)

Numerical variables depicted as median (25th percentile, 75th percentile)

3.3 Level of activity of the study participants

Mashipumelele had the greatest proportion of inactive participants (56.3%) who never walked a mile or more without stopping in the last month and 85.7% did no exercise in the preceding month compared to Khayelitsha - 44.8% never walked a mile or more without stopping in the last month and 77.9% did no exercise in the preceding month. In Oudtshoorn, 16.7% never walked a mile or more without stopping in the last month and 81.4% did no exercise in the preceding month and in Marconi Beam 54.6% never walked a mile or more without stopping in the last month and 82.58% did no exercise in the preceding month).

Table 3: Level of activity of the study participants

| | Khayelitsha (N =172) n (%) | Oudtshoorn (N = 156) n (%) | Marconi Beam (N = 132) n (%) | Mashipumelele (N = 112) n (%) | All areas (N = 572) n (%) |
|---|---|---|---|--|--|
| Frequency of walking a mile or more without stopping in the last month | | | | | |
| Never | 77 (44.8) | 26 (16.7) | 72 (54.6) | 63 (56.3) | 238 (41.6) |
| At least once per month | 95 (55.2) | 130 (83.3) | 60 (45.5) | 49 (43.8) | 334 (58.4) |
| Exercise done in past month | | | | | |
| No exercise | 134 (77.9) | 127 (81.41%) | 109 (82.6) | 96 (85.7) | 466 (81.5) |
| Exercised (jogging,cycling, swimming,aerobics, dancing,gardening,lift weights) | 38 (22.1) | 29 (18.59%) | 23 (17.4) | 16 (14.3) | 106 (18.5) |
| Number of times exercise per month (median p25 p75) | 3 (3 ,4) (n = 38) | 2 (2 ,3) (n = 29) | 3 (2 ,4) (n = 23) | 3 (2.5 ,4.5) (n = 16) | 3 (2,4) (n = 106) |

Categorical variables depicted as number (%)

Numerical variables depicted as median (25th percentile, 75th percentile)

3.4 Level of support and smoking habits of the study participants

Oudtshoorn had the greatest proportion of participants receiving emotional (97.4%) and financial support (95.5%). Furthermore, the proportion of participants from Oudtshoorn (32.1%) who smoked cigarettes was greater than those from Khayelitsha (9.3%), Marconi Beam (2.3%) and Mashipumelele (6.3%). The participants who smoked cigarettes, smoked a median of 6 cigarettes daily.

Table 4: Level of support and smoking habits of the study participants

| | Khayelitsha (N =172) n (%) | Oudtshoorn (N = 156) n (%) | Marconi Beam (N = 132) n (%) | Mashipumelele (N = 112) n (%) | All areas (N = 572) n (%) |
|--|---|---|---|--|--|
| Receiving Emotional Support | 115 (66.9) | 152 (97.4) | 78 (59.1) | 67 (59.8) | 412 (72.0) |
| Received emotional support within last 12 months | 165 (95.9) | 142 (91.0) | 125 (94.7) | 109 (97.3) | 541 (94.6) |
| Receiving financial support | 102 (59.3) | 149 (95.5) | 58 (43.9) | 55 (49.1) | 364 (63.6) |
| Smoke cigarettes | 16 (9.3) | 50 (32.1) | 3 (2.3) | 7 (6.3) | 76 (13.3) |
| Daily number of cigarettes smoked | 5 (3.5, 10) (n= 16) | 6.5 (4 ,15) (n = 50) | 4 (2 ,4) (n = 3) | 5 (2 ,5) (n = 5) | 6 (4 ,10) (n = 6) |
| Number of years smoking | 12 (6.5 ,22) (n = 16) | 20 (13 ,28) (n = 50) | 20 (5, 40) (n = 3) | 15 (8, 18) (n = 5) | 17 (10 ,25) (n = 6) |
| Pack years | 3.4 (2.2 ,4.9) (n = 16) | 5.5 (3 ,15) (n = 50) | 4 (1 ,4) (n = 3) | 1.8 (1.2, 4.5) (n = 5) | 4.3 (2.6, 12.6) (n = 6) |

Categorical variables depicted as number (%)

Numerical variables depicted as median (25th percentile, 75th percentile)

3.5 Cardiorespiratory outcomes of the study participants

More than 5% of the participants reported having been diagnosed with asthma by doctor (6.6%). Khayelitsha had the greatest proportion of participants who reported having experienced wheezing (22.1%), shortness of breath (17.4%) and tight chest (12.8%). Mashipumelele had the

greatest proportion of participants who reported having experienced shortness of breath after exercise (25.9%) and Khayelitsha's and Oudtshoorn's proportion of participants bringing up phlegm from the chest during winter (12.2% and 12.8% respectively) was greater than Marconi Beam's (2.3%) and Mashipumelele's (8.9%). Furthermore, all the participants reported experiencing at least one asthma symptom in the preceding year. Khayelitsha had the highest prevalence of self-reported chest pain followed by Oudtshoorn with the prevalence in both areas above 10%. Khayelitsha also had the highest prevalence of hypertension and cholesterol (15.1%, 25.0% and 9.3% respectively).

Table 5: Cardiorespiratory outcomes of the study participants

| | Khayelitsha (N =172) | Oudtshoorn (N = 156) | Marconi Beam (N = 132) | Mashipumelele (N = 112) | All areas (n = 572) |
|--|--|---------------------------------------|---|--|--------------------------------------|
| | n (%) | n (%) | n (%) | n (%) | n (%) |
| Doctor diagnosed asthma | 14 (8.1) | 11 (7.1) | 7 (5.3) | 6 (5.4) | 38 (6.6) |
| Wheezing in the last 12 months | 38 (22.1) | 20 (12.8) | 13 (9.9) | 21 (18.4) | 92 (16.1) |
| Shortness of breath in last 12 months | 30 (17.4) | 17 (10.9) | 8 (6.1) | 11 (9.8) | 66 (11.5) |
| Woken up by feeling of tight chest in the last 12 months | 22 (12.8) | 14 (9.0) | 9 (6.8) | 9 (8.0) | 54 (9.4) |
| Attack of shortness of breath at rest in the last 12 months | 18 (10.5) | 14 (9.0) | 7 (5.3) | 7 (6.3) | 46 (8.0) |
| Attack of shortness of breath after exercise in the last 12 months | 35 (20.4) | 26 (16.7) | 14 (10.6) | 29 (25.9) | 104 (18.2) |
| Woken up by attack of shortness of breath in the last 12 months | 18 (10.5) | 14 (9.0) | 7 (5.3) | 9 (8.0) | 48 (8.4) |
| Bring up phlegm from chest at any time of day in the winter | 21 (12.2) | 20 (12.8) | 3 (2.3) | 10 (8.9) | 53 (9.3) |
| Woken up by heavy coughing at any time in the last 12 months | 29 (16.9) | 22 (14.1) | 6 (4.6) | 16 (14.3) | 73 (12.8) |
| Self-reported asthma | 16 (9.3) | 11 (7.1) | 11 (8.3) | 6 (5.4) | 44 (7.7) |
| Medication for asthma control | 7 (4.1) | 10 (6.4) | 2 (1.5) | 1 (0.9) | 20 (3.5) |

| | | | | | |
|---|------------|------------|------------|-----------|------------|
| Asthma symptom score [#] | | | | | |
| • Score = 0 | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) |
| • Score = 1 | 109 (63.4) | 123 (78.9) | 111 (84.1) | 75 (67.0) | 418 (73.1) |
| • Score > 1 | 63 (36.6) | 33 (21.2) | 21 (15.9) | 37 (33.0) | 154 (26.9) |
| Affected by animals, dust or pollen from trees or flowers | 6 (3.5) | 6 (3.9) | 0 (0) | 0 (0) | 12 (2.1) |
| Self-reported experience chest pain | 26 (15.1) | 17 (10.9) | 5 (3.8) | 4 (3.6) | 52 (9.1) |
| Self-reported hypertension | 43 (25.0) | 38 (24.4) | 15 (11.4) | 21 (18.8) | 117 (20.5) |
| Self-reported cholesterol | 16 (9.3) | 5 (3.2) | 8 (6.1) | 5 (4.5) | 34 (5.9) |

[#]Asthma symptom score calculated as sum of: Wheezing in the last 12 months, Shortness of breath in last 12 months, woken up by feeling of tight chest in the last 12 months, Attack of shortness of breath at rest in the last 12 months, Attack of shortness of breath after exercise in the last 12 months, Woken up by attack of shortness of breath in the last 12 months, Self-reported asthma, Medication for asthma control

3.6 Summer, winter and annual levels of NO₂ and PM_{2.5}

NO₂ and PM_{2.5} levels were higher in winter (26.5µg/m³ and 13.4µg/m³ respectively) than summer (13.7µg/m³ and 7.7µg/m³ respectively). The mean annual NO₂ level was 20.5µg/m³ and the mean annual PM_{2.5} level was 10.8µg/m³.

Table 6: Descriptive summary of winter, summer and annual NO₂ and PM_{2.5} levels estimated at households of the participants in the study areas using land-use regression modelling.

| | Min | P₂₅ | P₅₀ | P₇₅ | Max | Mean (95% CI) |
|----------------------------------|------------|-----------------------|-----------------------|-----------------------|------------|----------------------|
| NO₂ (summer) | 2.4 | 4.4 | 16.8 | 18.3 | 35.8 | 13.7 (6.6-20.8) |
| NO₂ (winter) | 17.7 | 19.2 | 28.6 | 30.1 | 44.4 | 26.5 (20.6 – 32.3) |
| NO₂ (annual) | 12.5 | 13.3 | 22.4 | 24.1 | 39.9 | 20.5 (15.0 – 26.0) |
| PM_{2.5} (summer) | 0.1 | 5.4 | 8.1 | 9.6 | 16.7 | 7.7 (5.1-10.3) |
| PM_{2.5} (winter) | 2.2 | 10.1 | 12.9 | 17.2 | 26.6 | 13.4 (8.7-18.1) |
| PM_{2.5} (annual) | 4.3 | 8.7 | 10.6 | 13.1 | 28.0 | 10.8 (7.9-13.7) |

Min: minimum P25: 25th percentile P50: median P75: 75th percentile Max: maximum

3.7 Association between NO₂ levels and cardiorespiratory outcomes

A 10µg/m³ increase in annual NO₂ level was found to be significantly associated with a 2.9 (95%CI: 1.3 to 6.1) odds of having self-reported chest pain in the two-pollutant model.

Table 7: Association between a 10µg/m³ increase in NO₂ levels and cardiorespiratory outcomes (two-pollutant model)

| Outcome | Odds Ratio |
|--|----------------------------------|
| Doctor diagnosis of asthma | 1.0 (0.5-2.3) ^a |
| Asthma-symptom score ≥ 2 [*] | 1.0 (0.6-1.5) ^b |
| Self-reported chest pain | 2.9 (1.3-6.1)^c |
| Self-reported hypertension | 0.9 (0.5-1.6) ^d |
| Self-reported high cholesterol | 1.6 (0.7-3.6) ^e |

a: age, sex, smoke, affected by animals' dust or pollen from trees or flowers

b: age, sex smoke, brick house

c: age, sex, smoke, active in past month, receiving emotional support, receiving financial support

d: age, sex, smoke, active in past month, receiving emotional support, receiving financial support

e: age, sex, smoke

Bold text denotes statistical significance at $p < 0.05$

*Asthma symptom score calculated as sum of: Wheezing in the last 12 months, Shortness of breath in last 12 months, woken up by feeling of tight chest in the last 12 months, Attack of shortness of breath at rest in the last 12 months, Attack of shortness of breath after exercise in the last 12 months, Woken up by attack of shortness of breath in the last 12 months, Self-reported asthma, Medication for asthma control

3.8 Association between PM_{2.5} levels and cardiorespiratory outcomes

A 10µg/m³ increase in PM_{2.5} was found to be associated with a 0.4 odds of having two or more asthma symptoms in the two-pollutant model.

Table 8: Association between a 10ug/m³ increase in PM_{2.5} levels and cardiorespiratory outcomes (two-pollutant model)

| Outcome | Odds Ratio |
|----------------------------------|----------------------------------|
| Doctor diagnosis of asthma | 0.6 (0.1-2.7) ^a |
| Asthma-symptom score ≥ 2* | 0.4 (0.2-0.9)^b |
| Self-reported chest pain | 0.5 (0.1-2.1) ^c |
| Self-reported hypertension | 1.0 (0.8-2.7) ^d |
| Self-reported high cholesterol | 0.4 (0.1-1.7) ^e |

a: age, sex, smoke, born in town, affected by animals' dust or pollen from trees or flowers

b: age, sex, smoke, employed, damp spots inside house in last 12 months

c: age, sex, smoke, active in past month, receiving emotional support, receiving financial support

d: age, sex, smoke, receiving emotional support

e: age, sex, smoke, receiving financial support

Bold text denotes statistical significance at $p < 0.05$

*Asthma symptom score calculated as sum of: Wheezing in the last 12 months, Shortness of breath in last 12 months, woken up by feeling of tight chest in the last 12 months, Attack of shortness of breath at rest in the last 12 months, Attack of shortness of breath after exercise in the last 12 months, Woken up by attack of shortness of breath in the last 12 months, Self-reported asthma, Attack of asthma in last 12 months, Medication for asthma control

4. Discussion

This cross-sectional study conducted amongst adults from four informal settlement in the Western Cape found a positive association between NO₂ and the prevalence of self-reported chest pain (a surrogate for cardiovascular disease) adjusting for PM_{2.5} and other covariates. Although no association was found between PM_{2.5} and cardiorespiratory outcomes in the current study, there is laboratory evidence suggestive of the role of PM_{2.5} in increasing the absorption and transport of NO₂ into the human body, and thus resulting in a greater level of exposure to NO₂²¹. This is evident in the current study with the association between NO₂ and self-reported chest pain increasing from an odds of 2.80 to 2.92, when PM_{2.5} was included in the model, suggestive of an adjunct effect of NO₂ and PM_{2.5} on self-reported chest pain.

The average annual NO₂ estimated in all the four study areas were lower than the South African National Ambient Air Quality Standards (SAAQS) and the WHO Air Quality Guidelines of 40µg/m³^{1, 22, 2}. Thus the association of NO₂ with self-reported chest pain was found at levels lower than SAAQS and WHO air quality guidelines. The average annual PM_{2.5} level of 10.01µg/m³ is lower than the South African National Ambient Air Quality Standards (SAAQS) of 25µg/m³ but was similar to the WHO Air Quality guideline of 10µg/m³^{23,2}. Thus, the lack of association between PM_{2.5} and cardiorespiratory outcomes and of NO₂ with all cardiorespiratory outcomes except chest pain could thus be attributed to the fact that the pollutant levels were too low to exhibit hazardous effects. Furthermore, the sample size was also not powered enough to investigate the other associations, if indeed present.

In this current study, a 10µg/m³ increase in NO₂ was found to be associated with an almost three-fold increase in self-reported chest pain (OR: 2.92, 95% CI: 1.33 to 6.41). The number of significant associations were higher than what could be expected by chance for the number of comparisons made. A time-series study conducted in Canada amongst 157,028 adult participants found a 37.82µg/m³ increase in NO₂ levels to be associated with a 4% increased relative risk of having chest pain. The average NO₂ level in the Canadian study (37.82µg/m³) was greater than the observed 20.51µg/m³ in the current study²⁴. Furthermore, a cross-sectional study conducted amongst 26,991 women in Australia found no significant association between an interquartile range increase of 6.02µg/m³ in NO₂ () and chest pain (OR: 0.96, 99%CI 0.88 to 1.05)²⁵. The current and Canadian study therefore suggest that NO₂ can exert cardiovascular effects at levels lower than current local and international exposure limits. Furthermore, variables related to energy, transportation, and socio-economic factors have been shown to influence the association between NO₂ and various outcomes²⁶. The absence of adjustment for confounding variables such as household energy usage, transportation and socio-economic factors in the Canadian study could also explain the difference between effect size observed between the two studies. The lack of association between NO₂ and PM_{2.5} and respiratory outcomes is not consistent with the results of studies conducted in Eastern Estonia, Namibia, and Europe^{27,16,28,29}. The low levels of air pollutants, lack of objective outcome measures and inadequate sample size in this study could explain explain the number of non-significant associations.

According to the hygiene theory, children from rural areas or villages are exposed to more microbial substances which stimulate their immune systems and prevent them from developing asthma and other allergies later in life. Conversely, children born in urban areas are less exposed to these microbial substances and therefore have under stimulated immune systems in childhood which are hypersensitive and susceptible to various allergic disorders³⁰. Furthermore, animal dander and cigarette smoke are known precipitants of asthma and sleeping with the window open could suggest increased exposure to outdoor air pollutants and pollen (precipitants of asthma)^{31,32}. In the current study, demographic and household characteristics were therefore adjusted for in various models to mitigate the influence of residual confounding on the association between the air pollutants and respiratory outcomes.

Land use regression (LUR) models were used to estimate each participant's level of exposure to NO₂ and PM_{2.5} at the current address. The annual NO₂ LUR model explained 76% of the spatial variability in the NO₂ annual concentrations, 62% for the warm season and 77% for the cold season. The annual PM_{2.5} LUR model explained 29% of the spatial variability in the NO₂ annual concentrations, 36% for the warm season and 29% for the cold

season²⁰. The low spatial variation in PM_{2.5} could thus be an explanation for the lack of association between PM_{2.5} and the various cardiorespiratory outcomes as the observed measurements could be unrepresentative of each participant's true exposure.

The study had notable strengths. To the best of our knowledge, this is the only study conducted on the African continent using LUR modelling to determine the association between ambient air pollutants and cardiorespiratory outcomes in adults. Furthermore, the findings from the study can contribute to the paucity of results on the African continent investigating health effects of ambient air pollution and thus give a more representative reporting of the global burden of disease due to ambient air pollution. In the case of self-reported chest pain, non-cardiac causes of chest pain have been previously described, but this misclassification of outcome is likely non-differential across the exposure spectrum and would have only driven the association towards the null, if present. Furthermore, the cross-sectional nature of the study means that although inferences about associations can be made, the study cannot be used to make statements about causality and the fact that more than four fifths of the study participants were female, means that the observed associations could represent associations limited to females.

6. Conclusion

This study provided some preliminary evidence that exposure of adults to ambient NO₂ levels increases the odds of self-reported cardiovascular morbidity (chest pain) at levels below the SAAQS and the WHO Air Quality Guidelines. The presence of an association below these standards and guidelines suggest a revision of the current legislation to protect vulnerable population, especially those from informal settlements who might have underlying vulnerability and are disproportionately affected by the burden of air pollution. However, it is important to conduct further research amongst these population using more objective outcome and longitudinal study designs.

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8. Competing financial Interests

None

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PART D : APPENDICES

Appendix A : Questionnaire

Western Cape Air Pollution & Health Cohort Study

Adult Questionnaire

Cover sheet

A1. Date ____/____/____
Day Month Year

A2. Study Identification No. _____

A3. Study Area _____

A4. Interview time started

Time: __: __ am/pm

A5. Interviewer: Enter gender of
respondent

☐₁ Male ☐₂ Female

A. DEMOGRAPHICS

A6. How old are you? _____ years

A7. What is your date of birth?

_____/_____/_____
day month year

☐₉ Refused

A8. Are you the Head of Household?

☐₁ Yes

☐₂ No

A9. What is your race? I'll read the choices:

☐₁ African

☐₂ Indian

☐₃ Coloured

☐₄ White

☐₅ Other

(SPECIFY: _____)

☐₉ Refused

A10. What is the highest grade or year of school you completed? [READ CHOICES]

☐₁ Never attended school or only pre-school

☐₂ Primary school

☐₃ High school

☐₄ Higher Education

(College/Technikon/University)

☐₉ Refused

A11. In which town, province and country were you born?

_____; _____, _____
town province country

A12. What is your home language?

A13. Are you employed?

☐₁ Yes

☐₂ No

A14. How much on average do you earn monthly? _____

A15. How many people are working in this household? _____

B. RESIDENTIAL HISTORY

A16. Where do you stay? _____

A17. Please list all the places that you have lived and the number of years you lived there

| Places | Years |
|-----------------|-------|
| Philippi | |
| Khayelitsha | |
| Oudtshoorn | |
| Phoenix | |
| Joe Slovo | |
| Nyanga | |
| Milnerton | |
| Milnerton Ridge | |
| Others? _____ | |

C. RESPIRATORY HEALTH

I AM GOING TO ASK YOU SOME QUESTIONS. AT FIRST THESE WILL BE MOSTLY ABOUT YOUR BREATHING. WHEREVER POSSIBLE, I WOULD LIKE YOU TO ANSWER 'YES' OR 'NO'.

A18. Have you had wheezing or whistling in your chest at any time in the last 12 months? NO YES
☐ ☐

IF 'NO' GO TO QUESTION A19, IF 'YES':

A18.1. Have you been at all breathless when the wheezing noise was present? NO YES
☐ ☐

A18.2. Have you had this wheezing or whistling when you did *not* have a cold? NO YES
☐ ☐

A19. Have you woken up with a feeling of tightness in your chest at any time in the last 12 months? NO YES
☐ ☐

A20. Have you had an attack of shortness of breath that came on during the day when you were at rest at any time in the last 12 months? NO YES
☐ ☐

A21. Have you had an attack of shortness of breath that came on *following* strenuous activity at any time in the last 12 months? NO YES
☐ ☐

A22. Have you been woken by an attack of shortness of breath at any time in the last 12 months? NO YES
☐ ☐

IF NO GO TO A23, IF YES

A22.1 Have you been woken by an attack of shortness of breath in the last 3 months? NO YES
☐ ☐

IF NO GO TO A23, IF YES

A22.1.1 *On average* have you been woken by an attack of shortness of breath *at least once a week in the last 3 months?* NO YES
☐ ☐

IF NO GO TO A23, IF YES

A22.1.1.1 How many times a week *on average* have you been woken by shortness of breath in the *last 3 months?* TIMES

A23. Have you been woken by an attack of coughing at any time in the last 12 months? NO YES
☐ ☐

A24. Do you *usually* cough first thing in the morning in the winter? NO YES
☐ ☐
[IF DOUBTFUL, USE QUESTION A25.1 TO CONFIRM]

A25. Do you *usually* cough during the day, or at night, in the winter? NO YES
☐ ☐

IF 'NO' GO TO QUESTION A26, IF 'YES':

A25.1 Do you cough like this on most days for as much as three months each year?

NO YES
☐ ☐

A26. Do you *usually* bring up any phlegm from your chest first thing in the morning in the winter?

NO YES
☐ ☐

[IF DOUBTFUL, USE QUESTION A27.1 TO CONFIRM]

A27. Do you *usually* bring up any phlegm from your chest during the day, or at night, in the winter?

NO YES
☐ ☐

IF 'NO' GO TO QUESTION 28, IF 'YES':

A27.1 Do you bring up phlegm like this on most days for as much as three months each year?

NO YES
☐ ☐

A28. Do you ever have trouble with your breathing?

NO YES
☐ ☐

IF 'NO' GO TO QUESTION A29, IF 'YES':

A28.1 Do you have this trouble

TICK ONE BOX ONLY

- a) continuously so that your breathing is never quite right?
- b) repeatedly, but it always gets completely better?
- c) only rarely?

1 ☐
2 ☐
3 ☐

A29. Are you disabled from walking by a condition *other than* heart or lung disease?

NO YES
☐ ☐

IF 'YES' STATE CONDITION _____ AND GO TO QUESTION A30, IF 'NO':

A29.1 Are you troubled by shortness of breath when hurrying on level ground or walking up a slight hill?

NO YES
☐ ☐

IF 'NO' GO TO QUESTION A30, IF 'YES':

A29.1.1 Do you get short of breath walking with other people of your own age on level ground?

NO YES
☐ ☐

IF 'NO' GO TO QUESTION A30, IF 'YES':

A29.1.1.1 Do you have to stop for breath when walking at your own pace on level ground?

NO YES
☐ ☐

A30. FOR WOMEN ONLY - MEN GO TO A31

Have you ever noticed that you had respiratory symptoms (such as wheeze, tightness in your chest or shortness of breath) at a particular time of your monthly cycle?

TICK ONE BOX ONLY

- yes, in the week before my period
- yes, during my period
- yes, in the week after my period
- yes, another time of the month
- does not apply to me (i.e., amenorrhoeal)
- No

1 ☐
2 ☐
3 ☐
4 ☐
5 ☐
6 ☐

A31. Have you ever had asthma? NO YES
☐ ☐
IF 'NO' GO TO QUESTION A32, IF 'YES':

A31.1 Was this confirmed by a doctor? NO YES
☐ ☐
A31.2 How old were you when you had your first attack of asthma? YEARS

A31.3 How old were you when you had your most recent attack of asthma? YEARS

A31.4.1-6 Which months of the year do you usually have attacks of asthma?

| | NO | YES |
|------------------------------------|--------------------------|--------------------------|
| A31.4.1 January / February | <input type="checkbox"/> | <input type="checkbox"/> |
| A31.4.2 March / April | <input type="checkbox"/> | <input type="checkbox"/> |
| A31.4.3 May / June | <input type="checkbox"/> | <input type="checkbox"/> |
| A31.4.4 July / August | <input type="checkbox"/> | <input type="checkbox"/> |
| A31.4.5 September / October | <input type="checkbox"/> | <input type="checkbox"/> |
| A31.4.6 November / December | <input type="checkbox"/> | <input type="checkbox"/> |

A31.5 Have you had an attack of asthma in the last **12 months**? NO YES
☐ ☐
IF NO GO TO A31.8, IF YES
A31.6 How many attacks of asthma have you had in the last **12 months**? ATTACKS

A31.7 How many attacks of asthma have you had in the last **3 months**? ATTACKS

A31.8 How many times have you woken up because of your asthma in the last **3 months**? TICK ONE BOX ONLY

| | | |
|---|---|--------------------------|
| every night or almost every night | 1 | <input type="checkbox"/> |
| more than once a week, but not most nights | 2 | <input type="checkbox"/> |
| at least twice a month, but not more than once a week | 3 | <input type="checkbox"/> |
| less than twice a month | 4 | <input type="checkbox"/> |
| not at all | 5 | <input type="checkbox"/> |

A31.9. How often have you had trouble with your breathing because of your asthma in the last **3 months**? TICK ONE BOX ONLY

| | | |
|--|---|--------------------------|
| continuously | 1 | <input type="checkbox"/> |
| about once a day | 2 | <input type="checkbox"/> |
| at least once a week, but less than once a day | 3 | <input type="checkbox"/> |
| less than once a week | 4 | <input type="checkbox"/> |
| not at all | 6 | <input type="checkbox"/> |

A31.10 Are you currently taking any medicines including inhalers, aerosols or tablets for asthma? NO YES
☐ ☐

A31.11 Do you have a peak flow meter of your own? NO YES
☐ ☐
IF 'NO' GO TO QUESTION A31.12 , IF 'YES':

A31.11.1 How often have you used it over the last 3 months? TICK ONE BOX ONLY

| | | |
|------------------|---|--------------------------|
| never | 1 | <input type="checkbox"/> |
| some of the days | 2 | <input type="checkbox"/> |
| most of the days | 3 | <input type="checkbox"/> |

A31.12 Do you have written instructions from your doctor on how to manage your asthma if it gets worse or if you have an attack? NO YES
☐ ☐

A31.13 FOR WOMEN ONLY - MEN GO TO A32

Have you ever noticed that your asthma got worse with your monthly cycle? TICK ONE BOX ONLY

| | | |
|---|---|--------------------------|
| Yes, in the week before my period | 1 | <input type="checkbox"/> |
| Yes, during my period | 2 | <input type="checkbox"/> |
| Yes, in the week after my period | 3 | <input type="checkbox"/> |
| Yes, another time of the month | 4 | <input type="checkbox"/> |
| Does not apply to me (i.e., amenorrhoeal) | 5 | <input type="checkbox"/> |
| No | 6 | <input type="checkbox"/> |

A31.14 Have you been pregnant (at least 25 weeks) since your asthma started? NO YES
☐ ☐

IF NO GO TO A32, IF YES

A31.14.1.What happened to your asthma during your pregnancies?

TICK ONE BOX ONLY

| | | |
|----------------------------------|---|--------------------------|
| got better | 1 | <input type="checkbox"/> |
| got worse | 2 | <input type="checkbox"/> |
| stayed the same | 3 | <input type="checkbox"/> |
| not the same for all pregnancies | 4 | <input type="checkbox"/> |
| don't know | 5 | <input type="checkbox"/> |

D. OCCUPATIONAL HISTORY

I would now like to ask you some questions on the type of jobs that you have done.

I am interested in each one of the jobs that you have done for more than 3 consecutive months since the time we last contacted you (as regards the follow-up). These jobs may be outside the house or at home, full time or part time, paid or not paid, including self-employment, for example in a family business. Please include part time jobs only if you had been doing them for more than 8 hours per week.

A32. Are you currently

TICK ONE BOX ONLY

| | | |
|---------------------------------------|---|--------------------------|
| Employed (including military service) | 1 | <input type="checkbox"/> |
| Self employed | 2 | <input type="checkbox"/> |
| Unemployed, looking for work | 3 | <input type="checkbox"/> |
| Not working because of poor health | 4 | <input type="checkbox"/> |
| Full-time house-person | 5 | <input type="checkbox"/> |
| Full time student | 6 | <input type="checkbox"/> |
| Retired | 7 | <input type="checkbox"/> |
| Other | 8 | <input type="checkbox"/> |

IF EMPLOYED OR SELF EMPLOYED OR A FULL TIME HOUSEPERSON GO TO A34

A33. Have you been employed in any job for three continuous months or longer?

| NO | YES |
|--------------------------|--------------------------|
| <input type="checkbox"/> | <input type="checkbox"/> |

IF YES NOW GO TO OCCUPATIONAL MATRIX

A34. If you had more than one job in the same company, or if you were doing more than one job at the same time, we would like to talk about them separately. Please start with your current or last job.

| JOB | A34.1. What is (was) the title of your current (last) job? <i>OCCUPATION</i> | A34.2. What did the firm, company or organisation do or what services did it provide? <i>INDUSTRY</i> | A34.3. In what month and year did you start working in this job? | | | | A34.4. In what month and year did you stop working in this job? | | | | | | | | |
|--------|--|---|---|--|------|--|--|--|------|--|--|--|--|--|--|
| | | | MONTH | | YEAR | | MONTH | | YEAR | | | | | | |
| JOB 1 | | | | | | | | | | | | | | | |
| JOB 2 | | | | | | | | | | | | | | | |
| JOB 3 | | | | | | | | | | | | | | | |
| JOB 4 | | | | | | | | | | | | | | | |
| JOB 5 | | | | | | | | | | | | | | | |
| JOB 6 | | | | | | | | | | | | | | | |
| JOB 7 | | | | | | | | | | | | | | | |
| JOB 8 | | | | | | | | | | | | | | | |
| JOB 9 | | | | | | | | | | | | | | | |
| JOB 10 | | | | | | | | | | | | | | | |

A35. Have any of these jobs ever made your chest tight or wheezy?

NO YES
☐ ☐

IF YES, (tick no or yes for each job)

| | NO | YES |
|---------|--------------------------|--------------------------|
| Job 1? | <input type="checkbox"/> | <input type="checkbox"/> |
| Job 2? | <input type="checkbox"/> | <input type="checkbox"/> |
| Job 3? | <input type="checkbox"/> | <input type="checkbox"/> |
| Job 4? | <input type="checkbox"/> | <input type="checkbox"/> |
| Job 5? | <input type="checkbox"/> | <input type="checkbox"/> |
| Job 6? | <input type="checkbox"/> | <input type="checkbox"/> |
| Job 7? | <input type="checkbox"/> | <input type="checkbox"/> |
| Job 8? | <input type="checkbox"/> | <input type="checkbox"/> |
| Job 9? | <input type="checkbox"/> | <input type="checkbox"/> |
| Job 10? | <input type="checkbox"/> | <input type="checkbox"/> |

A36. Have you had to leave any of these jobs because they affected your breathing?

NO YES
☐ ☐

IF YES, (tick no or yes for each job)

| | NO | YES |
|---------|--------------------------|--------------------------|
| Job 1? | <input type="checkbox"/> | <input type="checkbox"/> |
| Job 2? | <input type="checkbox"/> | <input type="checkbox"/> |
| Job 3? | <input type="checkbox"/> | <input type="checkbox"/> |
| Job 4? | <input type="checkbox"/> | <input type="checkbox"/> |
| Job 5? | <input type="checkbox"/> | <input type="checkbox"/> |
| Job 6? | <input type="checkbox"/> | <input type="checkbox"/> |
| Job 7? | <input type="checkbox"/> | <input type="checkbox"/> |
| Job 8? | <input type="checkbox"/> | <input type="checkbox"/> |
| Job 9? | <input type="checkbox"/> | <input type="checkbox"/> |
| Job 10? | <input type="checkbox"/> | <input type="checkbox"/> |

E. INDOORS EXPOSURES

A37. When was your present home built?

| YEAR | | | |
|------|--|--|--|
| | | | |

A38. Which best describes the building in which you live?

- a) RDP house?
- b) a one family house detached from any other house?
- c) a one family house attached to one or more houses?
- d) a building for two families?
- e) a building for three or four families?
- f) a building for five or more families?
- h) an informal dwelling (shack)
- i) other: _____

TICK ONE BOX ONLY

| | |
|---|--|
| 1 | |
| 2 | |
| 3 | |
| 4 | |
| 5 | |
| 6 | |
| 7 | |
| 8 | |

A39. How many years have you lived in your current home

| YEARS | |
|-------|--|
| | |

A40. Does your home have air conditioning?

| NO | YES |
|----|-----|
| | |
| | |
| | |

A41. Which of the following appliances do you use for heating or for hot water?

A41.1 coal or wood fire

A41.2 gas heater/stove

A41.3 electric

heater/stove

A41.4 wood

heater/stove

A41.5 paraffin

heater/stove

A41.6 oil heater/stove

A41.7 coal heater/stove

A41.8 charcoal heater/stove

A 41.9 Cattle manure/animal dung heater/stove

A 41.10 Solar (sun) heater/stove

A41.11 other: _____

| NO | YES |
|----|-----|
| | |
| | |
| | |
| | |
| | |
| | |
| | |
| | |

A42. What kind of stove do you *mostly* use for cooking?

TICK ONE BOX ONLY

- a) coal, coke, charcoal or wood (solid fuel)?
- b) gas ?
- c) electric?
- d) paraffin (kerosene)?
- e) oil?
- f) Cattle manure/animal dung?
- g) Solar (sun)?

| | |
|---|--|
| 1 | |
| 2 | |
| 3 | |
| 4 | |
| 5 | |
| 6 | |
| 7 | |

h) other: _____

A42.1 IF YOU USE GAS FOR COOKING Which of the following do you have?

| NO | YES |
|--------------------------|--------------------------|
| <input type="checkbox"/> | <input type="checkbox"/> |
| <input type="checkbox"/> | <input type="checkbox"/> |

A42.1.1 gas hob

A42.1 2 gas oven

A43. What kind of stove was mostly used for cooking in the home you lived in when you were five years old?

TICK ONE BOX ONLY

- a) coal, coke or wood (solid fuel)?
- b) gas (gas from the mains)?
- c) electric?
- d) paraffin?
- e) gas (gas from bottles or other non-mains source)
- f) don't know
- g) other: _____

| | |
|---|--|
| 1 | |
| 2 | |
| 3 | |
| 4 | |
| 5 | |
| 6 | |
| 7 | |

A44. On average how long have you spent cooking with your stove each day over the *last four weeks*? MINUTES

| | | |
|--|--|--|
| | | |
|--|--|--|

A45. Over the last four weeks when you were cooking did you have a door or window to the outside air open

TICK ONE BOX ONLY

- a) most of the time
- b) some of time
- c) rarely (or only occasionally)
- d) I do not have a door or window that opens to the outside in my kitchen

| | |
|---|--|
| 1 | |
| 2 | |
| 3 | |
| 4 | |

A46. Do you have an extractor fan over the cooker?

| NO | YES | DK |
|--------------------------|--------------------------|--------------------------|
| <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |

IF 'NO' OR 'DON'T KNOW' GO TO QUESTION A47, IF 'YES':

A46.1 When cooking, do you use the fan

TICK ONE BOX ONLY

- a) all of the time?
- b) some of the time?
- c) none of the time?

| | |
|---|--|
| 1 | |
| 2 | |
| 3 | |

A46.2 Does the fan take the fumes outside the house?

| NO | YES | DK |
|--------------------------|--------------------------|--------------------------|
| <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |

A47. Does the room which you use most at home during the day

A47.1 have fitted carpets covering the whole floor?

A47.2 contain rugs?

A47.3 have double glazing windows?

NO YES

| | |
|--------------------------|--------------------------|
| <input type="checkbox"/> | <input type="checkbox"/> |
| <input type="checkbox"/> | <input type="checkbox"/> |
| <input type="checkbox"/> | <input type="checkbox"/> |

A48. How old is the oldest carpet or rug in the room which you use most at home during the day? ,

a) less than one year

b) 1-5 years old

c) more than 5 years old

TICK ONE BOX ONLY

| | |
|---|--------------------------|
| 1 | <input type="checkbox"/> |
| 2 | <input type="checkbox"/> |
| 3 | <input type="checkbox"/> |

A49. On what floor is the room which you use most at home during the day? (*The lowest floor of a building is 00*)

| | |
|----------------------|----------------------|
| <input type="text"/> | <input type="text"/> |
|----------------------|----------------------|

A50. Does your bedroom

A50.1 have fitted carpets covering the whole floor?

A50.2 contain rugs?

A50.3 have double glazing?

NO YES

| | |
|--------------------------|--------------------------|
| <input type="checkbox"/> | <input type="checkbox"/> |
| <input type="checkbox"/> | <input type="checkbox"/> |
| <input type="checkbox"/> | <input type="checkbox"/> |

A51. How old is the oldest carpet or rug in your bedroom

a) less than one year

b) 1-5 years old

c) more than 5 years old

TICK ONE BOX ONLY

| |
|--------------------------|
| <input type="checkbox"/> |
| <input type="checkbox"/> |
| <input type="checkbox"/> |

TICK ONE BOX ONLY

A52 How old is your mattress

a) less than one year

b) 1-5 years old

c) more than 5 years old

| |
|--------------------------|
| <input type="checkbox"/> |
| <input type="checkbox"/> |
| <input type="checkbox"/> |

A53. What floor of the building is your bedroom on? (lowest=00)

| | |
|----------------------|----------------------|
| <input type="text"/> | <input type="text"/> |
|----------------------|----------------------|

NO YES

A54. Do you sleep with the windows open at night during winter?

| | |
|--------------------------|--------------------------|
| <input type="checkbox"/> | <input type="checkbox"/> |
|--------------------------|--------------------------|

IF 'NO' GO TO QUESTION A55, IF 'YES':

A54.1 Do you sleep with the windows open

a) all of the time?

b) sometimes?

c) only occasionally?

TICK ONE BOX ONLY

| | |
|---|--------------------------|
| 1 | <input type="checkbox"/> |
| 2 | <input type="checkbox"/> |
| 3 | <input type="checkbox"/> |

A55. Has there been any water damage to the building or its contents,
NO

YES

DK for example,
from broken pipes,
leaks or floods?

IF YES

| | | |
|--------------------------|--------------------------|--------------------------|
| <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
|--------------------------|--------------------------|--------------------------|

NO

YES

DK **A55.1** Has there been any water damage in the last 12 months

A56. Within the last 12 months have you had wet or damp spots on surfaces inside your home other than in the basement (for example on walls, wall paper, NO

YES ceilings or carpets)?

A57. Has there ever been any mould or mildew on any surface, other than

NO YES DK food, inside the home?

IF 'NO' OR 'DON'T KNOW' GO TO QUESTION A58, IF 'YES':

A57.1.1-6 Which rooms have been affected?

NO YES **A57.1.1** bathroom(s)

A

5

7

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1

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A57.1.5 basement or attic

A57.1.6 other:

A57.2 Has

there been ☐

mould or

mildew on any

surfaces inside

the home

NO YES in

the last **12**

months?

F. OUTDOOR EXPOSURES

‘This scale looks like a thermometer; it allows you to rate your personal opinion regarding the following question on annoyance from air pollution. You can indicate your level of annoyance on this scale between 0 and 10 where 0 mean does not annoy at all' and 10 means intolerable annoyance.'

A58. How much are you annoyed by outdoor air pollution (from traffic, industry, etc.) if you keep the windows open?

| | | |
|--|----|-----------------------|
| | 10 | intolerable annoyance |
| | 9 | |
| | 8 | |
| | 7 | |
| | 6 | |
| | 5 | |
| | 4 | |
| | 3 | |
| | 2 | |
| | 1 | |
| | 0 | doesn't annoy at all |

A59. How often do cars pass your house?

TICK ONE BOX ONLY

- a) constantly
- b) frequently
- c) seldom
- d) never

| | |
|---|--------------------------|
| 1 | <input type="checkbox"/> |
| 2 | <input type="checkbox"/> |
| 3 | <input type="checkbox"/> |
| 4 | <input type="checkbox"/> |

A60. How often do heavy vehicles (e.g. trucks/buses) pass your house?

TICK ONE BOX ONLY

- a) constantly
- b) frequently
- c) seldom
- d) never

| | |
|---|--------------------------|
| 1 | <input type="checkbox"/> |
| 2 | <input type="checkbox"/> |
| 3 | <input type="checkbox"/> |
| 4 | <input type="checkbox"/> |

A61. Have you taken any of the following measures to reduce allergen or exposure to allergen in your home?

NO YES

A61.1 changed from carpet to a wooden or other smooth surface on floor of the room you use most

| | |
|--------------------------|--------------------------|
| <input type="checkbox"/> | <input type="checkbox"/> |
|--------------------------|--------------------------|

A61.2 changed from carpet to a wooden or to a smooth surface on floor of your bedroom

| | |
|--------------------------|--------------------------|
| <input type="checkbox"/> | <input type="checkbox"/> |
|--------------------------|--------------------------|

A61.3 bought a new carpet for the room you use most

| | |
|--------------------------|--------------------------|
| <input type="checkbox"/> | <input type="checkbox"/> |
|--------------------------|--------------------------|

A61.4 bought a new carpet for your bedroom

| | |
|--------------------------|--------------------------|
| <input type="checkbox"/> | <input type="checkbox"/> |
|--------------------------|--------------------------|

A61.5 used antidust-mite sprays

| | |
|--------------------------|--------------------------|
| <input type="checkbox"/> | <input type="checkbox"/> |
|--------------------------|--------------------------|

A61.6 put an allergy-proof cover on your mattress

| | |
|--------------------------|--------------------------|
| <input type="checkbox"/> | <input type="checkbox"/> |
|--------------------------|--------------------------|

A61.7 sold, given away or destroyed a pet dog or cat

| | |
|--------------------------|--------------------------|
| <input type="checkbox"/> | <input type="checkbox"/> |
|--------------------------|--------------------------|

A62. Do you keep a cat?

NO YES

| | |
|--------------------------|--------------------------|
| <input type="checkbox"/> | <input type="checkbox"/> |
|--------------------------|--------------------------|

IF 'NO' GO TO QUESTION A63, IF 'YES'

NO YES

62.1 Is your cat (are your cats) allowed inside the house?

| | |
|--------------------------|--------------------------|
| <input type="checkbox"/> | <input type="checkbox"/> |
|--------------------------|--------------------------|

62.2 Is your cat (are your cats) allowed in the bedroom?

| | |
|--------------------------|--------------------------|
| <input type="checkbox"/> | <input type="checkbox"/> |
|--------------------------|--------------------------|

NO YES

A63. Do you keep a dog?

NO YES

| | |
|--------------------------|--------------------------|
| <input type="checkbox"/> | <input type="checkbox"/> |
|--------------------------|--------------------------|

IF 'NO' GO TO QUESTION A64, IF 'YES':

NO YES

63.1 Is your dog (are your dogs) allowed inside the house?

| | |
|--------------------------|--------------------------|
| <input type="checkbox"/> | <input type="checkbox"/> |
|--------------------------|--------------------------|

63.2 Is your dog (are your dogs) allowed in your bedroom?

| | |
|--------------------------|--------------------------|
| <input type="checkbox"/> | <input type="checkbox"/> |
|--------------------------|--------------------------|

NO YES

A64. Do you keep any birds?

NO YES

| | |
|--------------------------|--------------------------|
| <input type="checkbox"/> | <input type="checkbox"/> |
|--------------------------|--------------------------|

IF 'NO' GO TO QUESTION A65, IF 'YES':

NO YES

64.1 Are any of these birds kept inside the house?

| | |
|--------------------------|--------------------------|
| <input type="checkbox"/> | <input type="checkbox"/> |
|--------------------------|--------------------------|

A65. Was there a cat in your home?

A65.1 during your first year of life

| | |
|--------------------------|--------------------------|
| <input type="checkbox"/> | <input type="checkbox"/> |
|--------------------------|--------------------------|

A65.2 when you were aged 1 to 4 years

| | |
|--------------------------|--------------------------|
| <input type="checkbox"/> | <input type="checkbox"/> |
|--------------------------|--------------------------|

A65.3 when you were aged 5-15 years

| | |
|--------------------------|--------------------------|
| <input type="checkbox"/> | <input type="checkbox"/> |
|--------------------------|--------------------------|

NO YES DK

A66. Was there a dog in

| |
|--------------------------|
| <input type="checkbox"/> |
| <input type="checkbox"/> |
| <input type="checkbox"/> |

your home? **A66.1** during your first year of life

A66.2 when you were aged 1 to 4 years

A66.3 when you were aged 5-15 years

| NO | YES | DK |
|--------------------------|--------------------------|--------------------------|
| <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |

A67. Was there a bird in your home?

A67.1 during your first year of life

| NO | YES | DK |
|--------------------------|--------------------------|--------------------------|
| <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |

A67.2 when you were aged 1 to 4 years

A67.3 when you were aged 5-15 years

A68. What term best describes the place you lived most of the time when you were under the age of five years?

TICK ONE BOX ONLY

- a) farm
- b) village in a rural area
- c) small town
- d) suburb of a city
- e) inner city

| | |
|---|--------------------------|
| 1 | <input type="checkbox"/> |
| 2 | <input type="checkbox"/> |
| 3 | <input type="checkbox"/> |
| 4 | <input type="checkbox"/> |
| 5 | <input type="checkbox"/> |

A69. When you are near animals, such as cats, dogs or horses, do you *ever*

A69.1 start to cough?

A69.2 start to wheeze?

A69.3 get a feeling of tightness in your chest?

A69.4 start to feel short of breath?

A69.5 get a runny or stuffy nose or start to sneeze?

A69.6 get itchy or watering eyes?

| NO | YES |
|--------------------------|--------------------------|
| <input type="checkbox"/> | <input type="checkbox"/> |
| <input type="checkbox"/> | <input type="checkbox"/> |
| <input type="checkbox"/> | <input type="checkbox"/> |
| <input type="checkbox"/> | <input type="checkbox"/> |
| <input type="checkbox"/> | <input type="checkbox"/> |
| <input type="checkbox"/> | <input type="checkbox"/> |

A70. When you are in a dusty part of the house, or near pillows or duvets do you *ever*

A70.1 start to cough?

A70.2 start to wheeze?

A70.3 get a feeling of tightness in your chest?

A70.4 start to feel short of breath?

| NO | YES |
|--------------------------|--------------------------|
| <input type="checkbox"/> | <input type="checkbox"/> |
| <input type="checkbox"/> | <input type="checkbox"/> |
| <input type="checkbox"/> | <input type="checkbox"/> |
| <input type="checkbox"/> | <input type="checkbox"/> |
| <input type="checkbox"/> | <input type="checkbox"/> |
| <input type="checkbox"/> | <input type="checkbox"/> |

A70.5 get a runny or stuffy nose or start to sneeze?

A70.6 get itchy or watering eyes?

A71. When you are near trees, grass or flowers, or when there is a lot of pollen about, do you *ever*

A71.1 start to cough?

A71.2 start to wheeze?

A71.3 get a feeling of tightness in your chest?

A71.4 start to feel short of breath?

A71.5 get a runny or stuffy nose or start to sneeze?

A71.6 get itchy or watering eyes?

IF 'YES' TO ANY OF THE ABOVE:

A71.7.1-4 Which time of year does this happen?

A71.7.1 winter

A71.7.2 spring

A71.7.3 summer

A71.7.4 autumn

NO YES

| | |
|--------------------------|--------------------------|
| <input type="checkbox"/> | <input type="checkbox"/> |
| <input type="checkbox"/> | <input type="checkbox"/> |
| <input type="checkbox"/> | <input type="checkbox"/> |
| <input type="checkbox"/> | <input type="checkbox"/> |
| <input type="checkbox"/> | <input type="checkbox"/> |
| <input type="checkbox"/> | <input type="checkbox"/> |

NO YES

| | |
|--------------------------|--------------------------|
| <input type="checkbox"/> | <input type="checkbox"/> |
| <input type="checkbox"/> | <input type="checkbox"/> |
| <input type="checkbox"/> | <input type="checkbox"/> |
| <input type="checkbox"/> | <input type="checkbox"/> |

G. CARDIOVASCULAR DISEASE

A72. Have you ever had any pain or discomfort in your chest?

| |
|--|
| |
| |
| |
| |

1

2

7

9

YES

NO (GO TO A80)

REFUSED (GO TO A80)

DON'T KNOW (GO TO A80)

A73. Do you get it when you walk uphill or

hurry?

| |
|--|
| |
| |
| |
| |
| |

1

2

3

7

9

YES

NO (GO TO A79)

NEVER WALKS UPHILL OR HURRIES

REFUSED (GO TO A79)

DON'T KNOW (GO TO A79)

A74. Do you get it when you walk at an ordinary pace on level ground?

| |
|--|
| |
| |
| |
| |

1

2

7

9

YES

NO

REFUSED

DON'T KNOW

A75. What do you do if you get it while you are walking? Do you stop or slow down, or continue at the same pace?

CODE "STOP OR SLOW DOWN" IF RESPONDENT CARRIES ON AFTER TAKING ISODIL (ISOSORBIDE DINITRATE).

| |
|--|
| |
| |
| |
| |

1

2

7

9

STOP OR SLOW DOWN

CONTINUE AT THE SAME PACE (GO TO A79)

REFUSED (GO TO A79)

DON'T KNOW (GO TO A79)

A76. If you stand still, what happens to it? Is the pain or discomfort relieved or not relieved?

| |
|--|
| |
| |
| |
| |

1

2

7

9

RELIEVED

NOT RELIEVED (GO TO A79)

REFUSED (GO TO A79)

DON'T KNOW (GO TO A79)

A77. How soon is the pain relieved? Would you say

| | |
|---|--|
| 1 | |
| 2 | |
| 7 | |
| 9 | |

10 minutes or less or
more than 10 minutes? (GO TO
A79)
REFUSED (GO TO A79)
DON'T KNOW (GO TO A79)

A78. Please look at this card and show me where the pain or discomfort is located.

CODE ALL THAT APPLY.
PROBE FOR ADDITIONAL AREAS.

HAND CARD CDQ1

| | |
|----|--|
| 1 | |
| 2 | |
| 3 | |
| 4 | |
| 5 | |
| 6 | |
| 7 | |
| 8 | |
| 77 | |
| 99 | |

1
2
3
4
5
6
7
8
REFUSED
DON'T KNOW

A79. Have you ever had a severe pain across the front of your chest lasting for half an hour or more?

| | |
|---|--|
| 1 | |
| 2 | |
| 7 | |
| 9 | |

YES
NO
REFUSED
DON'T KNOW

A80. Have you had shortness of breath either when hurrying on the level or walking up a slight hill?

| | | |
|---|--------------------------|------------|
| 1 | <input type="checkbox"/> | YES |
| 2 | <input type="checkbox"/> | NO |
| 7 | <input type="checkbox"/> | REFUSED |
| 9 | <input type="checkbox"/> | DON'T KNOW |

H. BLOOD PRESSURE

A81. Have you **ever** been told by a doctor or other health professional that you had hypertension (hy-per-**ten**-shun), also called high blood pressure?

IF HIGH BLOOD PRESSURE **ONLY** DURING PREGNANCY, CODE NO.

INTERVIEWER INSTRUCTION: IF RESPONDENT SAYS "HIGH NORMAL BLOOD PRESSURE", "BORDERLINE HYPERTENSION" OR "PREHYPERTENSION" CODE NO.

| | | |
|---|--------------------------|------------------------|
| 1 | <input type="checkbox"/> | YES |
| 2 | <input type="checkbox"/> | NO (GO TO A86) |
| 7 | <input type="checkbox"/> | REFUSED (GO TO A86) |
| 9 | <input type="checkbox"/> | DON'T KNOW (GO TO A86) |

HELP SCREEN:

Hypertension (High Blood Pressure): A repeatedly increased blood pressure with the first number 140 or higher and the second number 90 or higher.

A82. Were you told on 2 or more **different** visits that you had hypertension (hy-per-**ten**-shun), also called high blood pressure?

| | | |
|---|--------------------------|------------|
| 1 | <input type="checkbox"/> | YES |
| 2 | <input type="checkbox"/> | NO |
| 7 | <input type="checkbox"/> | REFUSED |
| 9 | <input type="checkbox"/> | DON'T KNOW |

A83. How were you when you were **first** told that you had hypertension or high blood pressure?

| | |
|----------------------|----------------------|
| <input type="text"/> | <input type="text"/> |
|----------------------|----------------------|

| | | |
|-----|--------------------------|------------|
| 777 | <input type="checkbox"/> | REFUSED |
| 999 | <input type="checkbox"/> | DON'T KNOW |

A84. Because of your (high blood pressure/hypertension) (hy-per-**ten**-shun), have you **ever** been told to **take prescribed medicine**?

| | | |
|---|--------------------------|------------------------|
| 1 | <input type="checkbox"/> | YES |
| 2 | <input type="checkbox"/> | NO (GO TO A86) |
| 7 | <input type="checkbox"/> | REFUSED (GO TO A86) |
| 9 | <input type="checkbox"/> | DON'T KNOW (GO TO A86) |

HELP SCREEN:

Prescribed Medicine: Prescribed medicines are those ordered by a doctor or other health provider through a written or verbal prescription for a pharmacist to fill. Prescription medicines can also be given by a medical provider directly to a patient to take home, such as free samples.

A85. Are you **now** taking a prescribed medicine?

| | | |
|---|--------------------------|------------|
| 1 | <input type="checkbox"/> | YES |
| 2 | <input type="checkbox"/> | NO |
| 7 | <input type="checkbox"/> | REFUSED |
| 9 | <input type="checkbox"/> | DON'T KNOW |

A86. Did you take your blood pressure at home during the last 12 months?

| | | |
|---|--------------------------|------------------------|
| 1 | <input type="checkbox"/> | YES |
| 2 | <input type="checkbox"/> | NO (GO TO A88) |
| 7 | <input type="checkbox"/> | REFUSED (GO TO A88) |
| 9 | <input type="checkbox"/> | DON'T KNOW (GO TO A88) |

A87. How often did you check your blood pressure at home during the last 12 months? (You can tell me the number of times per day, per week, per month, or per year.)

.....

ENTER NUMBER OF

TIMES

| | | |
|------|--------------------------|------------------------|
| 7777 | <input type="checkbox"/> | REFUSED (GO TO A88) |
| 9999 | <input type="checkbox"/> | DON'T KNOW (GO TO A88) |

.....
ENTER UNITS

| | | |
|---|--------------------------|-----------|
| 1 | <input type="checkbox"/> | PER DAY |
| 2 | <input type="checkbox"/> | PER WEEK |
| 7 | <input type="checkbox"/> | PER MONTH |
| 9 | <input type="checkbox"/> | PER YEAR |

A88. Did a doctor or other health professional tell you to take your blood pressure at home?

| | | |
|---|--------------------------|------------|
| 1 | <input type="checkbox"/> | YES |
| 2 | <input type="checkbox"/> | NO |
| 7 | <input type="checkbox"/> | REFUSED |
| 9 | <input type="checkbox"/> | DON'T KNOW |

A89. Have you **ever** been told by a doctor or other health professional that your blood cholesterol level was high?

| | | |
|---|--------------------------|-----------------|
| 1 | <input type="checkbox"/> | YES (GO TO A91) |
| 2 | <input type="checkbox"/> | NO |
| 7 | <input type="checkbox"/> | REFUSED |
| 9 | <input type="checkbox"/> | DON'T KNOW |

I. OTHER CHRONIC CONDITIONS

A90. Have you **ever** had your blood cholesterol checked?

| | | |
|---|--------------------------|------------|
| 1 | <input type="checkbox"/> | YES |
| 2 | <input type="checkbox"/> | NO |
| 7 | <input type="checkbox"/> | REFUSED |
| 9 | <input type="checkbox"/> | DON'T KNOW |

A91. Have you **ever** been told by a doctor or other health professional that you had diabetes?

| | | |
|---|--------------------------|------------|
| 1 | <input type="checkbox"/> | YES |
| 2 | <input type="checkbox"/> | NO |
| 7 | <input type="checkbox"/> | REFUSED |
| 9 | <input type="checkbox"/> | DON'T KNOW |

A92. Have you **ever** been told by a doctor or other health professional that you had congestive heart failure?

| | | |
|---|--------------------------|------------|
| 1 | <input type="checkbox"/> | YES |
| 2 | <input type="checkbox"/> | NO |
| 7 | <input type="checkbox"/> | REFUSED |
| 9 | <input type="checkbox"/> | DON'T KNOW |

A93. Have you **ever** been told by a doctor or other health professional that you had coronary heart disease?

| | | |
|---|--------------------------|------------|
| 1 | <input type="checkbox"/> | YES |
| 2 | <input type="checkbox"/> | NO |
| 7 | <input type="checkbox"/> | REFUSED |
| 9 | <input type="checkbox"/> | DON'T KNOW |

A94. Have you **ever** been told by a doctor or other health professional that you had angina?

| | | |
|---|--------------------------|------------|
| 1 | <input type="checkbox"/> | YES |
| 2 | <input type="checkbox"/> | NO |
| 7 | <input type="checkbox"/> | REFUSED |
| 9 | <input type="checkbox"/> | DON'T KNOW |

A95. Have you **ever** been told by a doctor or other health professional that you had heart attack (myocardial infarction)?

| | | |
|---|--------------------------|------------|
| 1 | <input type="checkbox"/> | YES |
| 2 | <input type="checkbox"/> | NO |
| 7 | <input type="checkbox"/> | REFUSED |
| 9 | <input type="checkbox"/> | DON'T KNOW |

A96. Have you **ever** been told by a doctor or other health professional that you had stroke?

| | | |
|---|--------------------------|------------|
| 1 | <input type="checkbox"/> | YES |
| 2 | <input type="checkbox"/> | NO |
| 7 | <input type="checkbox"/> | REFUSED |
| 9 | <input type="checkbox"/> | DON'T KNOW |

A97. Have you **ever** been told by a doctor or other health professional that you had emphysema?

| | | |
|---|--------------------------|------------|
| 1 | <input type="checkbox"/> | YES |
| 2 | <input type="checkbox"/> | NO |
| 7 | <input type="checkbox"/> | REFUSED |
| 9 | <input type="checkbox"/> | DON'T KNOW |

A98. Have you **ever** been told by a doctor or other health professional that you had thyroid?

| | | |
|---|--------------------------|------------|
| 1 | <input type="checkbox"/> | YES |
| 2 | <input type="checkbox"/> | NO |
| 7 | <input type="checkbox"/> | REFUSED |
| 9 | <input type="checkbox"/> | DON'T KNOW |

A99. Have you **ever** been told by a doctor or other health professional that you had chronic bronchitis?

| | | |
|---|--------------------------|------------|
| 1 | <input type="checkbox"/> | YES |
| 2 | <input type="checkbox"/> | NO |
| 7 | <input type="checkbox"/> | REFUSED |
| 9 | <input type="checkbox"/> | DON'T KNOW |

A100. Have you **ever** been told by a doctor or other health professional that you had tuberculosis?

| | | |
|---|--------------------------|------------|
| 1 | <input type="checkbox"/> | YES |
| 2 | <input type="checkbox"/> | NO |
| 7 | <input type="checkbox"/> | REFUSED |
| 9 | <input type="checkbox"/> | DON'T KNOW |

J. PHYSICAL ACTIVITY

A101. In the past month, how often did you walk a mile or more at a time without stopping?

| | | |
|-----------------------------|-------|-----------------------------------|
| <input type="text"/> | times | <input type="checkbox"/> _1 day |
| number | per | <input type="checkbox"/> _2 week |
| | | <input type="checkbox"/> _3 month |
| <input type="checkbox"/> _0 | never | |

The next questions are about your leisure time physical activity during the past month. We are interested in the following exercises, sports, or physically active hobbies that you might have done.

A102. In the past month, did you do any physical activity such as jogging, cycling, swimming, aerobics, dancing, gardening or lift weights?

| | |
|-----------------------------|-----------------|
| <input type="checkbox"/> _1 | Yes |
| <input type="checkbox"/> _2 | No [GO TO A108] |

If yes, what were these activities?

A103. Activity 1:

How often did you participate in them?

| | | |
|----------------------|-------|-----------------------------------|
| <input type="text"/> | times | <input type="checkbox"/> _1 day |
| number | per | <input type="checkbox"/> _2 week |
| | | <input type="checkbox"/> _3 month |

A104. Activity 2

| | | |
|----------------------|-------|-----------------------------------|
| <input type="text"/> | times | <input type="checkbox"/> _1 day |
| number | per | <input type="checkbox"/> _2 week |
| | | <input type="checkbox"/> _3 month |

A105. Activity 3

| | | |
|----------------------|-------|-----------------------------------|
| <input type="text"/> | times | <input type="checkbox"/> _1 day |
| number | per | <input type="checkbox"/> _2 week |
| | | <input type="checkbox"/> _3 month |

A106. Activity 4

| | | |
|----------------------|-------|-----------------------------------|
| <input type="text"/> | times | <input type="checkbox"/> _1 day |
| number | per | <input type="checkbox"/> _2 week |
| | | <input type="checkbox"/> _3 month |

A107. Activity 5

_____ times ☐₁ day
number per ☐₂ week
☐₃ month

A108. How does the amount of activity that you stated above for the past month compare with your physical activity for the past 12 months?

- ☐₁ more active
☐₂ less active
☐₃ about the same
☐₈ don't know

A109. Compared with yourself 10 years ago, would you say you were more or less active now?

- ☐₁ more active
☐₂ less active
☐₃ about the same
☐₈ don't know

K. PSYCHO-SOCIAL STRESS

Now I would like to ask a few questions about your friends, family, home and work

A110. Can you count on anyone to provide you with emotional support such as taking over problems or helping you make a difficult decision?

- | | | |
|---|--------------------------|------------------------------|
| 1 | <input type="checkbox"/> | YES |
| 2 | <input type="checkbox"/> | NO (GO TO A112) |
| 3 | <input type="checkbox"/> | DON'T NEED HELP (GO TO A112) |
| 7 | <input type="checkbox"/> | REFUSED (GO TO A112) |
| 9 | <input type="checkbox"/> | DON'T KNOW (GO TO A112) |

A111. In the last 12 months, could you have used more emotional support than you received?

- | | | |
|---|--------------------------|------------|
| 1 | <input type="checkbox"/> | YES |
| 2 | <input type="checkbox"/> | NO |
| 7 | <input type="checkbox"/> | REFUSED |
| 9 | <input type="checkbox"/> | DON'T KNOW |

A112. If you need some extra help financially, could you count on anyone to help; for example, by paying any bills, housing costs, hospital visits, or providing you with food and clothes?

| | | |
|---|--------------------------|-----------------------------|
| 1 | <input type="checkbox"/> | YES |
| 2 | <input type="checkbox"/> | NO |
| 3 | <input type="checkbox"/> | OFFERED HELP BUT I WOULDN'T |
| 7 | <input type="checkbox"/> | ACCEPT IT |
| 9 | <input type="checkbox"/> | REFUSED |
| | | DON'T KNOW |

A113. In the last 12 months, do you feel stressed at work?

| | | |
|---|--------------------------|------------|
| 1 | <input type="checkbox"/> | YES |
| 2 | <input type="checkbox"/> | NO |
| 7 | <input type="checkbox"/> | REFUSED |
| 9 | <input type="checkbox"/> | DON'T KNOW |

L. TOBACCO USE

Cigarette use

A114. Have you smoked at least 100 cigarettes during your entire life (equivalent to about 5 packs)? ☐₁ Yes ☐₂ No [GO TO A126]

A115. How old were you when you first started smoking cigarettes fairly regularly? _____ Age In Years

A116. Do you smoke cigarettes now? ☐₁ Yes ☐₂ No [GO TO A120]

A117. About how many cigarettes do you smoke per day? _____ number

A118. For approximately how many years have you smoked this amount? _____ years

A119. Was there ever a period of a year or more when you smoked more than [number in A117] cigarettes per day? ☐₁ Yes ☐₂ No

A120. During the period when you were smoking the most, about how many cigarettes per day did you usually smoke? _____ number ☐₁ cigarettes per day ☐₂ packs per day

☐₀ less than 1 per day
☐₉₈ varied

A121. For how many years did you smoke that amount? _____ years
number

A122. Have you ever quit smoking for a period of one year or longer? ☐₁ Yes ☐₂ No

A123. Since you first started smoking; how many years altogether have you stayed off cigarettes? ☐₀ never quit smoking
☐₇₇ less than one year
_____ years
number

A124. About how old were you when you last smoked cigarettes (fairly regularly)? _____
age

A125. About how many cigarettes per day did you usually smoke at that time?

☐₈ don't know
☐₉₈ currently smoking [GO TO A127]
☐₀ less than 1 per day

_____ ☐₁ cigarettes per day
number ☐₂ packs per day

A126. Did you quit smoking because you had a health problem that was caused or made worse by smoking?

☐₉₈ varied
☐₁ Yes
☐₂ No
☐₈ Don't know

Other Tobacco Use

A127. Have you ever smoked a pipe regularly? ☐₁ Yes
YES means more than 350grams of tobacco ☐₂ No [GO TO A129]

in a lifetime

A128. How much pipe tobacco are you smoking now? [On the average over the entire time you smoked pipes, how many grams did you smoke per week?] _____ grams per week

Cigar Use

A129. Have you ever smoked cigars regularly? ☐₁ Yes
Yes means more than 1 cigar a week for a year ☐₂ No [END]

A130. On the average over the entire time you smoked cigars, how many cigars did you smoke per week? _____ Cigars per week

THANK YOU FOR COMPLETING THIS QUESTIONNAIRE!

END: Thank you for helping us!

Interview completed at:

Time: __:__ am / pm

[INTERVIEWER: Indicate quality of interview

☐₁ reliable

☐₂ unreliable]

Appendix B: Informed Consent

Consent to participate in a survey investigating cardiopulmonary health effects in adults due to exposures to ambient air pollution and other environmental pollutants in the Western Cape

1. Title of research project

An Epidemiological Cohort of Adult Investigating Cardiopulmonary Outcomes Following Exposure to Ambient Air Pollution and Other Environmental Pollutions

2. Name of researchers

Mohamed Aqiel Dalvie (BSc, Honours, MSc, PhD)

Mohamed Jeebhay (MbChB, MMED, PhD)

Rajen Naidoo (MbChB, MMED, PhD)

Toyib Adedamola Olaniyan (BSc Hons., MSc)

Purpose of the research project

The Department of Environmental Health and Development Planning, is conducting this survey investigating the effect of air pollution and other environmental pollutants on cardiopulmonary health in adults. This study is necessary and important because air pollution in the Western Cape is significant and could result in adverse health effects. We would like to interview you on your own health during this year (2016). The study will benefit residents in the Western Cape exposed to air pollution and other environmental pollutants.

3. Description of the research project

We will interview you once at your home for about 15 minutes.

The testing will include:

- a) **Questionnaires:** A member of our study team will interview you in privacy to complete a questionnaire. You will be asked questions about your breathing or chest problems; current and previous employment history; smoking habit (if any); home environment; and questions on your use of medications and health services.

4. Risks and discomforts of the research

There are minimal risks associated with completing the questionnaire. The only risk is a loss of confidentiality about personal information but the data will be seen only by study personnel. All reports will present aggregate data in which individuals will not be identifiable.

6. Expected benefits to you and to others

If any questions are found through the questionnaire, then you will be referred to your practitioner or local clinic for further management.

The results of the study would help you and others know the risks associated with various occupational and environmental pollutions for adults. This would further allow you to manage and/or reduce your risk. A copy of the final report of the study will be made available at the school that your child attends as the school is part of the children study. Additionally, an information sheet on the risks of air pollution and how to manage these risks will be distributed to you. A seminar on the results of the study and the managing of the risks of air pollution will be held at the school after the completion of the study.

The results obtained from this questionnaire at large would help the government of the Western Cape know the degree to which health is affected by environmental pollution. This would further help in further planning in reducing environmental exposures in residential areas.

7. Costs to you resulting from participation in the study

The study is offered at no cost to you. In the event a problem is discovered and you wish to be seen by a doctor for it, we can recommend to you who to see. However, the study cannot pay for these additional medical visits or treatments.

8. Confidentiality of information collected

Your and your child's name will not appear in any reports on this study. The records from the questionnaires will be kept completely confidential and will be seen only by members of the study team.

9. Documentation of the consent

One copy of this signed document will be kept together with our research records for this study. A copy of the information sheet about the study will be given to you to keep.

10. Contact person.

You may contact one of the following persons for answers to further questions about the research, your rights, or any injury you may feel is related to the study.

Name of person: MA Dalvie (The principal investigator) telephone 021 4066610

Name of person: Lamees Emjedi (Ethics administrator) telephone 021 4066492

11. Voluntary nature of participation

Your participation in this project is voluntary. Subsequent to your consent, you

may refuse to participate in or withdraw from the study at any time without penalty or loss of benefits to which you may otherwise be entitled.

9. Consent of the participant

I have read the information given above, or it has been read to me. I understand the meaning of this information. By signing this form, I hereby consent to participate in the study. I also understand that I am free to withdraw from the study at any time without penalty.

Printed name of participant

Signature, Mark, or Thumb Print

Interviewer's name (Print)

Signature

Witness (Print) (If caregiver is illiterate)

Signature

DATE: _____

Appendix C: Ethics approval letter



UNIVERSITY OF CAPE TOWN

Faculty of Health Sciences



Human Research Ethics Committee

Room E53-46 Old Main Building Groote Schuur Hospital Observatory 792

Telephone [021] 406 649 Email: sumay.h.aflefdlen@uct.ac.za website:

www.health.uct.ac.za/fhs/research/humanethics/form

29 October 2018

HREC REF: 639/2018

Prof A Dalvie

School of Public Health & Family Medicine Room 4.31, 4th Floor

Falmouth Building FHS

Dear Prof Dalvie

PROJECT TITLE: AMBIENT AIR POLLUTION AND CARDIO RESPIRATORY OUTCOMES IN THE

WESTERN CAPE IN 2016 (SUB-STUDY LINKED TO 234/2009) - Masters Candidate: Dr H Bagula

Thank you for submitting your study to the Faculty of Health Sciences Human Research Ethics Committee (HREC) for review.

It is a pleasure to inform you that the HREC has formally approved the above-mentioned study.

Approval is granted for one year until the 30 November 2019.

Please submit a progress form, using the standardised Annual Report Form if the study continues beyond the approval period. Please submit a Standard Closure form if the study is completed within the approval period.

(Forms can be found on our website: www.health.uct.ac.za/fhs/research/humanethics/forms)

We acknowledge that the student: Dr Herman Bagula will also be involved in this study.

Please quote the HREC REF in all your correspondence.

Please note that the ongoing ethical conduct of the study remains the responsibility of the principal investigator.

Please note that for all studies approved by the HREC, the principal Investigator obtain appropriate Institutional approval, where necessary, before the research may occur.

Yours sincerely

Signature removed

PROFESSOR M BLOCKMAN
CHAIRPERSON, FHS HUMAN RESEARCH ETHICS COMMITTEE

Yours sincerely

Federal Wide Assurance Number: MA00001637.

Institutional Review Board (IRB) number: IRB00001938

This serves to confirm that the University of Cape Town Human Research Ethics Committee complies to the Ethics Standards for Clinical Research with a new drug in patients, based on the Medical Research Council (MRC-SA), Food and Drug Administration (FDA-USA), International Convention on

Harmonisation Good Clinical Practice (ICH GCP), South African Good Clinical Practice Guidelines (Doy 2006), based on the Association of the British Pharmaceutical Industry Guidelines (ABPI), and Declaration of Helsinki (2013) guidelines.

The Human Research Ethics Committee granting this approval is in compliance with the ICH

Harmonised Tripartite Guidelines E6: Note for Guidance on Good Clinical Practice (CPMP/ICH/135/95) and FDA Code Federal Regulation Part 50, 56 and 312.

Appendix D: Bivariate association between covariates and cardio respiratory outcomes

| | Doctors diagnosed asthma | Asthma score | Wheezing in the last 12 months | Shortness of breath in last 12 months | Woken up by feeling of tight chest in the last 12 months | Attack of shortness of breath at rest in the last 12 months | Attack of shortness of breath after exercise in the last 12 months | Woken up by attack of shortness of breath in the last 12 months |
|----------------------|--------------------------------|-------------------------------|--------------------------------------|--|---|---|---|--|
| Variable Name | Odds ratio | Odds ratio | Odds ratio | Odds ratio | Odds ratio | Odds ratio | Odds ratio | Odds ratio |
| Age | 1.05(1.02 – 1.09)*** | 1.02(0.99 – 1.04)* | 1.03(1.00 – 1.05)** | 1.04(1.01 – 1.07)*** | 1.04(1.01 – 1.07)*** | 1.04(1.00 – 1.07)*** | 1.02(0.99 – 1.04) | 1.05(1.02 – 1.08)*** |
| Sex(male) | 0.76(0.18 – 3.29) | 1.75(0.96 – 3.19)* | 1.24(0.56 – 2.76) | 1.38(0.58 – 3.39) | 1.31(0.49 – 3.48) | 0.61(0.14 – 2.62) | 1.53(0.93 – 3.17) | 0.93(0.28 – 3.15) |
| Higher education | 1.32(0.60 – 2.90) | 3.00(1.94 – 4.65)**** | 1.97(1.16 – 3.36) | 1.49(0.81 – 2.74) | 2.02(1.02 – 4.00)** | 1.55(0.74 – 3.23) | 2.81(1.62 – 4.89)**** | 1.87(0.88 – 3.96) |
| Xhosa | 1.80(0.75 – 4.30) | 8.73(4.69 – 16.23)**** | 6.59(2.97 – 14.63)**** | 4.84(2.03 – 11.54)**** | 8.84(2.70 – 28.90)**** | 3.59(1.37 – 9.41)*** | 4.26(2.20 – 8.25)**** | 2.98(1.22 – 7.29)** |
| Current Residence | 3.09(1.40 – 6.80)**** | 3.63(2.34 – 5.65)**** | 3.80(2.26 – 6.42)**** | 3.62(1.98 – 6.61)**** | 3.13(1.64 – 5.99)*** | 3.91(1.92 – 7.98)**** | 2.33(1.37 – 3.94)**** | 4.79(2.38 – 9.65)**** |
| Occupation | | | | | | | | |
| Employed | 1.32(0.61 – 2.87) | 1.94(1.31 – 2.87)*** | 1.75(1.07 – 2.86)** | 1.00(0.55 – 1.85) | 1.16(0.61 – 2.21) | 0.83(0.29 – 1.77) | 1.59(0.98 – 2.57)* | 1.76(0.88 – 3.50) |

| | | | | | | | | |
|---------------------------------------|-------------------------------|--------------------------------|--------------------------------|--------------------------------|--------------------------------|-----------------------------|--------------------------------|--------------------------------|
| Job Duration | 1(0.99 – 1.00) | 1(1.00 – 1.00) | 1.00(0.98 – 1.01) | 0.99(0.96 – 1.02) | 1.00(0.99 – 1.00) | 1.00(0.98 – 1.02) | 1.00(1.00 – 1.00) | 1.00(1.00 – 1.00) |
| Indoor exposure | | | | | | | | |
| Brick house | 3.63(1.67 – 7.92)*** | 2.18(1.47 – 3.24)**** | 2.34(1.43 – 3.83)*** | 2.28(1.28 – 4.07)*** | 1.57(0.84 – 2.95) | 2.98(1.48 – 6.00)*** | 1.66(1.02 – 2.69)** | 3.58(1.78 – 7.21)**** |
| Shack | 1.69(0.73 – 3.95) | 1.75(1.12 – 2.74)** | 1.77(1.02 – 3.08)** | 1.64(0.85 – 3.14)* | 2.05(1.05 – 4.00)** | 1.29(0.57 – 2.92) | 1.23(0.70 – 2.18) | 0.84(0.34 – 2.08) |
| Other than brickhouse or shack | 1(-) | 1(-) | 1(-) | 1(-) | 1(-) | 1(-) | 1(-) | 1(-) |
| Air conditioning | 2.34(0.52 – 10.63) | 11.00(3.92 – 30.86)**** | 4.07(1.57 – 10.57)*** | 3.83(1.33 – 11.00)** | 2.29(0.65 – 8.15) | 1.88(0.42 – 8.47) | 5.80(2.32 – 14.48)**** | 1.82(0.41 – 8.18) |
| Electricity | 12.69(1.71 – 94.06)*** | 21.45(7.80 – 59.02)**** | 19.06(4.62 – 78.58)**** | 25.00(3.43 – 182.26)*** | 21.09(2.88 – 154.25)*** | 1(-) | 21.02(5.10 – 86.54)**** | 16.28(2.21 – 119.76)*** |
| Time Spent Cooking | 1.27(0.90 – 1.81) | 1.00(0.80 – 1.27) | 1.25(0.96 – 1.63)* | 1.42(1.05 – 1.91)** | 1.21(0.89 – 1.65) | 1.42(1.03 – 1.97)** | 0.91(0.67 – 1.21) | 1.43(1.03 – 1.98)** |
| Electricity at 5 years | 1.21(0.50 – 2.92) | 1.30(0.84 – 2.04) | 1.29(0.73 – 2.26) | 1.57(0.83 – 2.96) | 1.07(0.51 – 2.22) | 2.07(0.99 – 4.30)* | 1.44(0.85 – 2.46) | 1.48(0.69 – 3.17) |
| Wood or coal at 5 years | 3.26(1.51 – 7.00)*** | 1.53(1.00 – 2.34)** | 2.05(1.23 – 3.42)*** | 1.75(0.95 – 3.21)* | 1.30(0.66 – 2.56) | 1.72(0.83 – 3.56)* | 1.02(0.59 – 1.75) | 1.64(0.79 – 3.38) |

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| Gas at 5 years | 1.71(0.21 – 13.64) | 2.11(0.68 – 6.54) | 0.58(0.07 – 4.53) | 1(-) | 2.33(0.50 – 10.87) | 1(-) | 1.96(0.53 – 7.29) | 1.34(0.17 – 10.62) |
| Paraffin at 5 years | 0.76(0.18 – 3.29) | 2.74(1.54 – 4.88)*** | 1.69(0.81 – 3.52) | 2.01(0.89 – 4.53)* | 1.65(0.66 – 4.10) | 0.61(0.14 – 2.62) | 2.51(1.30 – 4.87)*** | 2.72(1.13 – 6.57)** |
| Let air in most of time | 10.54(4.71 – 23.58)*** | 3.58(2.04 – 6.30)**** | 3.68(1.95 – 6.92)**** | 3.49(1.70 – 7.15)*** | 3.22(1.50 – 6.94)*** | 4.66(2.10 – 10.33)**** | 2.38(1.24 – 4.60)** | 6.11(2.85 – 13.04)**** |
| Let air in some time | 0.98(0.44 – 2.16) | 1.55(1.05 – 2.29)** | 1.32(0.80 – 2.16) | 1.05(0.58 – 1.90) | 0.91(0.47 – 1.73) | 0.96(0.46 – 1.98) | 1.44(0.90 – 2.33)* | 0.91(0.45 – 1.88) |
| Let air in rarely | 0.49(0.11 – 2.10) | 3.39(2.07 – 5.55)**** | 2.00(1.08 – 3.69)** | 2.19(1.09 – 4.38)** | 3.93(2.00 – 7.72)**** | 2.12(0.92 – 4.86)* | 4.53(2.62 – 7.81)**** | 2.04(0.89 – 4.66)* |
| Use of extractor fan | 5.37(1.08 – 26.54)** | 5.14(1.43 – 18.47)** | 7.46(2.11 – 26.44)*** | 4.79(1.20 – 19.10)** | 5.68(1.41 – 22.77)888 | 4.31(0.88 – 21.15)* | 2.82(0.71 – 11.15)* | 7.39(1.83 – 29.94)*** |
| Carpets or rugs | 3.33(1.53 – 7.25)*** | 1.75(1.11 – 2.74)*** | 1.64(0.94 – 2.86)* | 1.64(0.85 – 3.14)* | 1.82(0.92 – 3.60)* | 2.39(1.15 – 4.99)** | 1.23(0.70 – 2.18) | 2.28(1.10 – 4.74)** |
| Double glazing | 6.95(0.70 – 69.04) | 1.10(0.11 – 10.68) | 2.36(0.24 – 23.00) | 1(-) | 4.24(0.43 – 41.64) | 5.63(0.57 – 55.57)* | 1(-) | 1(-) |
| Age of Oldest Carpet(More than 5 years) | 3.03(0.65 – 14.05) | 1.52(0.52 – 4.54) | 1.65(0.46 – 5.93) | 2.55(0.70 – 9.25) | 1.82(0.40 – 8.29) | 4.07(1.10 – 15.04)** | 3.05(1.03 – 9.02)** | 3.94(1.07 – 14.52)** |

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| Sleeping with open window | 0.55(0.25 – 1.24)* | 0.50(0.33 – 0.74)*** | 0.4(0.23 – 0.69)*** | 1.60(0.93-2.72)* | 1.52(0.85-2.70) | 1.58(0.85-2.93) | 2.99(1.93-4.63)**** | 0.53(0.26 – 1.10)* |
| Sleep with open windows at night | 4.96(0.47 – 36.82) | 3.36(0.67 – 16.16.82)* | 1.41(0.16 – 12.24) | 2.15(0.25 – 18.78) | 6.50(1.16 – 36.52)** | 3.36(0.38 – 29.62) | 6.64(1.32 – 33.47)** | 3.26(0.37 – 28.68) |
| Water damage to building or its content | 1.54(0.57 – 4.18) | 4.91(2.97 – 8.13)**** | 3.13(1.75 – 5.62)**** | 3.35(1.73 – 6.49)**** | 3.74(1.88 – 7.44)** | 2.26(0.98 – 5.21) | 4.22(2.42 – 7.35)**** | 3.54(1.66 – 7.58)*** |
| Water damage in last 12 months | 1.98(0.72 – 5.41) | 4.44(2.58 – 7.67)**** | 2.91(1.55 – 5.48)*** | 2.71(1.31 – 5.61)*** | 4.39(2.15 – 8.94)**** | 2.43(1.09 – 5.84)** | 3.85(2.11 – 6.99)**** | 3.38(1.50 – 7.59)*** |
| Damp spots inside house in last 12 months | 1.91(0.79 – 4.64)* | 4.07(2.55 – 6.51)**** | 3.25(1.87 – 5.63)**** | 3.51(1.88 – 6.57)**** | 3.23(1.65 – 6.30)*** | 2.46(1.14 – 5.34)** | 3.09(1.80 – 5.21)**** | 3.17(1.52 – 6.63)** |
| Outdoor exposure | | | | | | | | |
| Intervention to reduce allergen | 3.59(1.38 – 9.35)*** | 3.41(1.85 – 6.31)**** | 2.42(1.17 – 5.00)** | 3.43(1.59 – 7.41)** | 2.99(1.30 – 6.89)** | 4.23(1.79 – 9.97)*** | 3.20(1.62 – 6.30)*** | 4.06(1.73 – 9.55)*** |

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| Pets | 5.17(2.32 – 11.52)**** | 3.88(3.34 – 6.43)**** | 4.15(2.34 – 7.34)**** | 5.84(3.12 – 10.95)**** | 2.58(1.24 – 5.35)** | 3.77(1.76 – 8.11)*** | 3.37(1.91 – 5.95)**** | 7.27(3.54 – 14.92)**** |
| Born in Village | 1(-) | 0.48(0.18 – 1.26)* | 0.59(0.18 – 1.95) | 0.91(0.27 – 3.06) | 1.08(0.32 – 3.65) | 0.91(0.21 – 3.95) | 0.53(0.16 – 1.78) | 0.88(0.20 – 3.82) |
| Born in town | 1.71(0.77 – 3.78) | 1.13(0.73 – 1.73) | 1.51(0.90 – 2.57)* | 1.41(0.76 – 2.63) | 1.28(0.65 – 2.51) | 1.46(0.70 – 3.08) | 0.99(0.58 – 1.71) | 0.60(0.24 – 1.48) |
| Born in suburb | 1(-) | 1.68(0.56 – 4.99) | 0.50(0.06 – 3.82) | 0.76(0.10 – 5.87) | 3.28(0.89 – 12.09)* | 1.18(0.15 – 9.26) | 2.41(0.75 – 7.75)* | 1(-) |
| Affected by animals, dust or pollen from trees or flowers | 4.78(0.96 – 23.92)* | 8.36(2.00 – 34.94)*** | 5.35(1.30 – 22.04)** | 0.07(0.01 – 0.36)*** | 7.19(0.82 – 63.00)* | 8.94(2.13 – 37.43)*** | 4.63(0.93 – 23.15)* | 5.28(1.39 – 20.09)** |
| Exercise | | | | | | | | |
| Walking | 0.55(0.26 – 1.18) | 0.88(0.60 – 1.31) | 0.49(0.30 – 0.80)*** | 0.56(0.31 – 1.00)** | 1.23(0.64 – 2.38) | 0.70(0.35 – 1.42) | 1.38(0.83 – 2.30) | 0.58(0.29 – 1.15)* |
| Active in past month | 1.07(0.36 – 3.18) | 3.30(2.02 – 3.40)**** | 2.16(1.18 – 3.95)* | 1.89(0.93 – 3.86)* | 3.86(1.97 – 7.58)*** | 2.06(0.91 – 4.78)* | 2.52(2.52 – 4.47)*** | 3.77(1.79 – 7.92)**** |
| Frequency of physical activity | 1.00(0.83 – 1.20) | 0.97(0.88 – 1.07) | 0.97(0.84 – 1.12) | 0.99(0.88 – 1.12) | 0.97(0.84 – 1.13) | 0.69(0.37 – 1.30) | 0.96(0.82 – 1.12) | 0.98(0.86 – 1.13) |

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| Physical activity 10 years ago | 1.68(0.79 – 3.60) | 4.27(2.86 – 6.39)**** | 2.93(1.78 – 4.83)**** | 4.06(2.19 – 7.53)**** | 3.14(1.66 – 5.94)**** | 4.29(2.00 – 9.14)**** | 5.48(3.24 – 9.25)**** | 4.49(2.11 – 9.53)**** |
| Psychosocial | | | | | | | | |
| Receiving Emotional support | 1.72(0.80 – 3.71) | 4.13(2.74 – 6.24)**** | 4.01(2.34 – 6.91)**** | 3.34(1.79 – 6.25)**** | 5.49(2.59 – 11.65)**** | 4.43(1.97 – 9.96)**** | 3.71(2.21 – 6.20)**** | 5.51(2.37 – 12.84)**** |
| Receiving emotional support within last 12 months | 1.72(0.80 – 3.71) | 4.13(2.74 – 6.24)**** | 4.02(2.34 – 6.91)**** | 3.34(1.79 – 6.25)**** | 5.50(2.59 – 11.65)**** | 4.43(1.97 – 9.96)**** | 3.71(2.21 – 6.20)**** | 5.51(2.37 – 12.84) |
| Receiving financial support | 1.54(0.72 – 3.30) | 2.53(1.72 – 3.73)**** | 2.53(1.72 – 3.73)**** | 2.43(1.48 – 3.98)**** | 2.49(1.39 – 4.45)*** | 2.45(1.32 – 4.57)*** | 2.63(1.30 – 5.33)*** | 2.17(1.09 – 4.30)** |
| Tobacco Use | | | | | | | | |
| Smoking | 1.60(0.36 – 7.10) | 4.16(1.93 – 8.97)**** | 3.65(1.59 – 8.41)** | 5.91(2.52 – 13.87)**** | 2.94(1.06 – 8.15)** | 2.07(0.59 – 7.24) | 2.74(1.17 – 6.46)** | 3.88(1.38 – 10.93)** |

*denotes significance at p<0.15

**denotes significance at p<0.05

***denotes significance at p<0.01

****denotes significance at p<0.001

| | Bring up phlegm from chest at any time of day in the winter | Woken up by heavy coughing at any time in the last 12 months | Attack of asthma in last 12 months | Medication for asthma control | Self- reported asthma | Chest Pain | Hypertension | High Blood Cholesterol |
|-------------------|--|--|---|-------------------------------------|-----------------------------|------------------------------|-------------------------------|------------------------------|
| Variable Name | Odds ratio | Odds ratio | Odds ratio | Odds ratio | Odds ratio | Odds ratio | Odds Ratio | Odds ratio |
| Age | 1.00(0.96 – 1.03) | 1.02(0.99 – 1.04) | 0.98(0.93 – 1.03) | 1.06(1.02 – 1.11)*** | 1.04(1.01 – 1.08)*** | 1.02(0.99 – 1.05) | 1.08(1.05 – 1.11)**** | 1.07(1.04 – 1.11)**** |
| Sex(male) | 2.13(0.84 – 5.36)* | 1.60(0.68 – 3.74) | 1(-) | 1(-) | 0.96(0.29 – 3.27) | 1.68(0.62 – 4.50)* | 1.11(0.50 – 2.45) | 2.10(0.77 – 5.74)* |
| Higher education | 3.17(1.37 – 7.37)*** | 3.40(1.68 – 6.91)*** | 0.61(0.19 – 2.00) | 0.60(0.18 – 1.97) | 1.79(0.84 – 3.81) | 1.95(0.92 – 4.12)* | 1.63(0.99 – 2.68) | 1.26(0.59 – 2.70) |
| Xhosa | 3.09(1.26 – 7.54)** | 2.38(1.20 – 4.74)** | 0.76(0.23 – 2.49) | 0.70(0.21 – 2.31) | 2.35(1.00 – 5.49)*** | 6.95(2.10 – 22.90)*** | 5.54(2.71 – 11.33)**** | 5.59(1.67 – 18.64)*** |
| Current Residence | 2.38(1.15 – 4.91)** | 3.08(1.69 – 5.61)**** | 0.74(0.20 – 2.75) | 3.84(1.15 – 12.81)** | 2.60(1.25 – 5.41)** | 4.53(2.27 – 9.05)**** | 3.70(2.22 – 6.14)**** | 4.32(2.04 – 9.15)**** |

| Occupation | | | | | | | | |
|---------------------------------------|--------------------------------|--------------------------------|-----------------------------|------------------------------|------------------------------|--------------------------------|--------------------------------|-------------------------------|
| Employed | 1.15(0.57 – 2.32) | 1.14(0.63 – 2.05) | 0.57(0.19 – 1.72) | 0.75(0.20 – 2.87) | 1.27(0.62 – 2.58) | 1.48(0.74 – 2.93) | 1.22(0.75 – 1.98) | 1.18(0.55 – 2.52) |
| Job Duration | 0.99(0.96 – 1.02) | 1.00(1.00 – 1.00) | 1.00(0.99 – 1.00) | 0.96(0.87 – 1.07) | 1.00(0.99 – 1.00) | 0.98(0.94 – 1.02) | 1.00(0.98 – 1.01) | 0.98(0.95 – 1.02) |
| Indoor exposure | | | | | | | | |
| Brick house | 1.83(0.92 – 3.61)* | 1.94(1.09 – 3.43)** | 0.38(0.13 – 1.15)* | 3.95(1.14 – 13.66)** | 3.39(1.67 – 6.87)*** | 2.32(1.18 – 4.57)** | 2.76(1.71 – 4.44)**** | 1.73(0.82 – 3.64) |
| Shack | 1.40(0.64 – 3.07) | 0.95(0.46 – 1.96) | 0.54(0.16 – 1.78) | 1.56(0.41 – 5.97) | 2.07(0.98 – 4.38)* | 1.90(0.91 – 3.98)* | 1.54(0.89 – 2.65)* | 2.53(1.17 – 5.48)** |
| Other than brickhouse or shack | 1(-) | 1(-) | 1(-) | 1(-) | 1(-) | 1(-) | 1(-) | 1(-) |
| Air conditioning | 5.84(1.99 – 17.11)*** | 1.85(0.52 – 6.53) | 0.41(0.05 – 3.28) | 1(-) | 1.88(0.42 – 8.47) | 2.89(0.81 – 10.37) | 1.12(0.32 – 3.92) | 2.17(0.48 – 9.80) |
| Electricity | 16.80(2.29 – 123.51)*** | 26.14(3.59 – 190.47)*** | 0.18(0.02 – 1.43)* | 4.50(0.57 – 35.40) | 7.58(1.80 – 31.47)*** | 16.80(2.29 – 123.57)*** | 21.35(5.19 – 87.89)**** | 13.70(1.85 – 101.31)** |
| Time Spent Cooking | 1.29(0.94 – 1.79)* | 1.03(0.75 – 1.42) | 0.91(0.51 – 1.60) | 1.22(0.71 – 2.08) | 1.24(0.88 – 1.73) | 1.03(0.70 – 1.50) | 0.99(0.75 – 1.30) | 0.81(0.50 – 1.31) |
| Electricity at 5 years | 1.42(0.67 – 3.02) | 1.19(0.62 – 2.30) | 1.54(0.34 – 7.03) | 1.36(0.36 – 5.20) | 1.54(0.72 – 3.32) | 1.64(0.78 – 3.43) | 0.65(0.35 – 1.23) | 0.54(0.19 – 1.58) |
| Wood or coal at 5 years | 1.37(0.65 – 2.85) | 0.99(0.51 – 1.90) | 0.20(0.06 – 0.61)*** | 5.54(1.60 – 19.19)*** | 2.41(1.44 – 5.87)** | 1.01(0.47 – 2.21) | 2.12(1.30 – 3.48)*** | 1.56(0.71 – 3.41) |

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| Gas at 5 years | 1.30(0.16 – 10.29) | 1.89(0.41 – 8.76) | 0.25(0.03 – 2.11) | 1(-) | 1.38(0.17 – 10.47) | 1(-) | 0.52(0.07 – 4.07) | 1(-) |
| Paraffin at 5 years | 2.13(0.84 – 5.36)* | 2.63(1.24 – 5.58)** | 0.54(0.12 – 2.51) | 1(-) | 0.61(0.14 – 2.62) | 4.49(2.04 – 9.92)**** | 2.20(1.12 – 4.32)** | 2.69(1.05 – 6.90)** |
| Let air in most of time | 2.51(1.04 – 6.02)** | 2.89(1.39 – 5.99)*** | 0.11(0.04 – 0.34)**** | 12.79(3.77 – 43.43)**** | 11.56(5.48 – 24.37)**** | 3.04(1.31 – 7.03)** | 3.23(1.73 – 6.04)**** | 2.57(1.00 – 6.58)* |
| Let air in some time | 1.63(0.83 – 3.20) | 1.79(1.02 – 3.16)** | 3.18(0.70 – 14.50)* | 1.48(0.45 – 4.91) | 0.83(0.40 – 1.75) | 1.13(0.57 – 2.26) | 2.68(1.66 – 4.31)**** | 1.58(0.76 – 3.30) |
| Let air in rarely | 2.73(1.26 – 5.90)** | 2.63(1.35 – 5.10) | 0.84(0.18 – 3.84) | 1(-) | 0.86(0.30 – 2.17) | 3.17(1.49 – 6.73)*** | 1.16(0.60 – 2.25) | 2.08(0.86 – 5.02) |
| Use of extractor fan | 4.04(0.83 – 19.89) | 2.61(0.54 – 12.63) | 0.19(0.02 – 1.61)* | 6.38(0.74 – 55.20)* | 7.65(1.89 – 31.00)*** | 4.04(0.83 – 19.78)* | 2.78(0.70 – 10.98) | 2.13(0.26 – 17.36) |
| Carpets or rugs | 2.50(1.22 – 5.09)** | 0.95(0.46 – 1.96) | 0.38(0.12 – 1.18)* | 7.61(2.19 – 26.45)** | 2.75(1.33 – 5.67)*** | 2.84(1.41 – 5.75)*** | 1.79(1.05 – 3.05)** | 1.54(0.67 – 3.54) |
| Double glazing | 5.29(0.54 – 52.13) | 1(-) | 1(-) | 1(-) | 5.63(0.57 – 55.57)* | 5.28(0.54 – 51.13) | 1(-) | 1(-) |
| Age of Oldest Carpet(More than 5 years) | 2.29(0.50 – 10.47) | 2.44(0.67 – 8.84) | 1(-) | 3.79(0.46 – 31.50) | 2.44(0.53 – 11.19) | 5.69(1.74 – 18.63)*** | 2.17(0.68 – 6.90) | 1.26(0.16 – 9.89) |
| Sleeping with open window | 0.51(0.11 – 1.26) | 0.71(0.39 – 1.26) | 1.90(0.58 – 6.24) | 0.68(0.20 – 2.35) | 0.41(0.19 – 0.90)** | 0.44(0.21 – 0.93)* | 0.32(0.19 – 0.55)**** | 0.23(0.09 – 0.60)*** |
| Sleep with open windows at night | 3.16(0.36 – 27.79) | 2.06(0.24 – 17.98) | 1(-) | 11.56(1.24 – 108.17)** | 3.63(0.38 – 29.62) | 3.16(0.36 – 27.79) | 1.27(0.15 – 11.01) | 3.86(0.44 – 34.08) |

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| Water damage to building or its content | 2.09(0.92 – 4.78)* | 4.84(2.59 – 9.05)**** | 0.79(0.17 – 3.64) | 2.66(0.69 – 10.69) | 1.52(0.81 – 2.55) | 4.52(2.18 – 9.38)**** | 2.29(1.26 – 4.13)**** | 2.70(1.15 – 6.30)** |
| Water damage in last 12 months | 1.83(0.73 – 4.59) | 4.77(2.46 – 9.23)**** | 0.62(0.13 – 2.87) | 3.39(0.88 – 13.15)* | 1.97(0.78 – 4.96) | 4.47(2.08 – 9.62)**** | 2.83(1.53 – 5.25)*** | 3.51(1.49 – 8.26)*** |
| Damp spots inside house in last 12 months | 3.48(1.69 – 7.15)*** | 4.42(2.41 – 8.08)**** | 2.20(0.28 – 17.13) | 3.26(0.93 – 11.36)* | 1.47(0.62 – 3.48) | 3.98(1.95 – 8.05)**** | 2.22(1.27 – 3.87)** | 4.09(1.90 – 8.82)**** |
| Outdoor exposure Intervention to reduce allergen | 3.91(1.67 – 9.17)*** | 4.36(2.10 – 9.07)**** | 0.27(0.07 – 1.00)* | 2.72(0.57- 12.99) | 2.79(1.09 – 7.12)** | 5.58(2.50 – 12.46)**** | 3.53(1.81 – 6.89)**** | 6.10(2.61 – 14.27)**** |
| Pets | 4.00(1.91 – 8.40)**** | 4.00(2.12 – 7.59)**** | 0.31(0.09 – 1.03)* | 9.09(2.70 – 30.58)**** | 4.38(2.07 – 9.29)**** | 2.97(1.37 – 6.44)*** | 3.59(2.05 – 6.31)**** | 2.26(0.93 – 5.46)* |
| Born in Village | 1.36(0.40 – 4.65) | 0.55(0.13 – 2.35) | 1(-) | 1(-) | 1(-) | 0.40(0.05 – 3.02) | 0.96(0.36 – 2.53) | 0.49(0.07 – 3.70) |
| Born in town | 1.34(0.64 – 2.79) | 0.76(0.38 – 1.53) | 1.86(0.41 – 8.50) | 2.54(0.76 – 8.45)* | 1.68(0.81 – 3.49) | 1.34(0.64 – 2.79) | 1.13(0.67 – 1.92) | 1.30(0.58 – 2.90) |
| Born in suburb | 1.11(0.14 – 8.69) | 1.59(0.35 – 7.25) | 1(-) | 1(-) | 1(-) | 2.47(0.53 – 11.37) | 1.61(0.44 – 5.82) | 1(-) |
| Affected by animals, dust or pollen from trees or flowers | 28.00(7.08 – 110.28)**** | 11.20(2.65 – 47.40)*** | 6.86(1.69 – 27.82)*** | 5.89(1.54 – 22.44)*** | 5.59(1.36 – 23.07)** | 6.63(1.60 – 27.50)*** | 2.09(0.25 – 17.22) | 5.36(1.41 – 20.39)** |
| Exercise | | | | | | | | |

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|--|-------------------------------|-------------------------------|---------------------------|----------------------------|---------------------------|-----------------------------|------------------------------|-------------------------------|
| Walking | 0.88(0.44 – 1.77) | 1.22(0.67 – 2.23) | 1.10(0.36 – 3.42) | 0.47(0.14 – 1.54) | 0.55(0.27 – 1.10)* | 1.00(0.50 – 2.02) | 0.85(0.53 – 1.37) | 0.98(0.46 – 2.10) |
| Active in past month | 2.68(1.24 – 5.80)** | 2.30(1.17 – 4.52)** | 0.51(0.14 – 1.89) | 1(-) | 1.41(0.56 – 3.51) | 3.12(1.55 – 6.62)*** | 1.90(1.05 – 3.44)** | 1.30(0.48 – 3.51) |
| Frequency of physical activity | 1.00(0.90 – 1.12) | 0.85(0.67 – 1.26) | 1.02(0.76 – 1.37) | - | 0.99(0.83 – 1.18) | 0.98(0.85 – 1.14) | 1.06(0.96 – 1.16) | 0.99(0.81 – 1.20) |
| Physical activity 10 years ago | 3.55(1.74 – 7.26)*** | 3.59(1.98 – 6.51)**** | 0.37(0.12 – 1.15)* | 2.93(0.85 – 10.12)* | 1.69(0.85 – 3.39)* | 3.12(1.55 – 6.29)*** | 2.18(1.36 – 3.50)*** | 5.89(2.48 – 13.96)**** |
| Psychosocial | | | | | | | | |
| Receiving Emotional support | 4.09(1.89 – 8.87)**** | 5.53(2.79 – 10.97)**** | 0.93(0.31 – 2.79) | 1.05(0.32 – 3.48) | 1.86(0.92 – 3.77)* | 3.52(1.67 – 7.44)*** | 4.70(2.75 – 8.02)**** | 3.10(1.40 – 6.90)*** |
| Receiving emotional support within last 12 months | 4.09(1.89 – 8.87)**** | 5.53(2.79 – 10.97)**** | 0.93(0.31 – 2.79) | 1.05(0.32 – 3.48) | 1.86(0.92 – 3.76)* | 3.52(1.67 – 7.44)*** | 4.70(2.75 – 8.02)**** | 3.10(1.40 – 6.90)*** |
| Receiving financial support | 2.59(1.30 – 5.13)*** | 2.47(1.39 – 4.37)*** | 0.67(0.22 – 2.00) | 1.46(0.44 – 4.14) | 1.59(0.79 – 3.18) | 1.80(0.92 – 3.55)* | 2.48(1.54 – 3.99)**** | 3.19(1.49 – 6.84)*** |
| Tobacco Use | | | | | | | | |
| Smoking | 7.69(3.11 – 18.97)**** | 4.63(1.93 – 11.11)*** | 0.58(0.07 – 4.66) | 4.76(0.98 – 23.16)* | 1.28(0.29 – 5.65) | 2.78(0.91 – 8.50)* | 3.87(1.72 – 8.72)*** | 4.70(1.65 – 13.40)*** |

Appendix E: Single and two pollutant association between a 10µg/m³ increase in NO₂ levels and cardiorespiratory outcomes

| | NO ₂ summer | | NO ₂ winter | | NO ₂ annual | |
|--------------------------------|-------------------------------------|-------------------------------------|-------------------------------------|-------------------------------------|-------------------------------------|-------------------------------------|
| | Single pollutant | Two pollutant | Single pollutant | Two Pollutant | Single Pollutant | Two Pollutant |
| Doctor diagnosis of asthma | 1.02(0.53-1.79) ^{1a} | 1.21(0.58-2.51) ^{1b} | 0.84(0.44-1.72) ^{1c} | 0.90(0.43-1.98) ^{1d} | 1.01(0.41-2.09) ^{1e} | 1.01(0.51-2.32) ^{1f} |
| Asthma-symptom score ≥ 2* | 0.92(0.62-1.34) ^{2a} | 1.11(0.69-1.62) ^{2b} | 1.00(0.71-1.54) ^{2c} | 1.11(0.73-1.61) ^{2d} | 0.82(0.52-1.22) ^{2e} | 1.00(0.60-1.51) ^{2f} |
| Self-reported chest pain | 2.71(1.50-5.18)^{3a} | 2.49(1.17-4.88)^{3b} | 2.28(1.19-4.38)^{3c} | 2.32(1.24-4.49)^{3d} | 2.80(1.34-5.90)^{3e} | 2.92(1.33-6.14)^{3f} |
| Self-reported hypertension | 0.92(0.63-1.29) ^{4a} | 0.81(0.38-1.31) ^{4b} | 1.00(0.58-1.62) ^{4c} | 1.00(0.62-1.61) ^{4d} | 0.79(0.56-1.62) ^{4e} | 0.93(0.52-1.62) ^{4f} |
| Self-reported high cholesterol | 1.18(0.62-2.31) ^{5a} | 1.31(0.61-2.83) ^{5b} | 1.33(0.61-2.64) ^{5c} | 1.39(0.72-2.81) ^{5d} | 1.32(0.58-2.91) ^{5e} | 1.61(0.73-3.63) ^{5f} |

Bold text denotes statistical significance at p < 0.05

Appendix F displays list of confounders included in each model

*Asthma symptom score calculated as sum of: Wheezing in the last 12 months, Shortness of breath in last 12 months, woken up by feeling of tight chest in the last 12 months, Attack of shortness of breath at rest in the last 12 months, Attack of shortness of breath after exercise in the last 12 months, Woken up by attack of shortness of breath in the last 12 months, Self-reported asthma, Medication for asthma control

Appendix F: List of confounders included in the models investigating the association between NO₂ levels and cardio respiratory outcomes

| | A | b | c | d | e | f |
|----------|--|---|--|--|---|---|
| 1 | age, sex, smoke, damp spots inside house in last 12 months, born in town, affected by animals dust or pollen from trees or flowers | age, sex, smoke | age, sex, smoke, brick house, damp spots inside house in last 12 months, intervention to reduce allergen, affected by animals dust or pollen from trees or flowers | age, sex, smoke, damp spots inside house in last 12 months, born in town, affected by animals dust or pollen from trees or flowers | Age, sex, smoke, born in town, affected by animals dust or pollen from trees or flowers | age, sex, smoke, affected by animals dust or pollen from trees or flowers |
| 2 | age, sex, smoke, current residence, brick house | age, sex, smoke, affected by animals dust or pollen from trees or flowers | age, sex, smoke, brick house, electricity | age, sex, smoke, brick house | age, sex, smoke, brick house, damp spots inside house in last 12 months | age, sex smoke, brick house |
| 3 | age, sex, smoke, current residence, active in past month, receiving financial support | age, sex, smoke, active in past month, receiving emotional support, receiving financial support | age, sex, smoke, brick house, active in past month, receiving financial support | Age, sex, smoke, active in past month, receiving emotional support, receiving financial support | age, sex, smoke, active in past month, receiving financial support | age, sex, smoke, active in past month, receiving emotional support, receiving financial support |
| 4 | age, sex, smoke, current residence, active in past month, receiving emotional support | age, sex, smoke, active in past month, receiving emotional support | age, sex, smoke, active in past month, receiving emotional support | age, sex, smoke, receiving, receiving emotional support | age, sex, smoke, active in past month, receiving emotional support, receiving financial support | age, sex, smoke, active in past month, receiving emotional support, receiving financial support |
| 5 | age, sex, smoke, receiving emotional support, receiving, financial support | age, sex, smoke, active in past month, receiving financial support | age, sex, smoke, receiving financial support | age, sex, smoke, receiving, receiving emotional support, receiving financial support | age, sex, smoke, receiving emotional support, receiving financial support | age, sex, smoke |

Appendix G: Single- and two-pollutant association between a 10µg/m³ increase in PM_{2.5} levels and cardiorespiratory outcomes

| | PM _{2.5} summer | | PM _{2.5} winter | | PM _{2.5} annual | |
|--------------------------------|--------------------------------|-------------------------------|-------------------------------|-------------------------------|-------------------------------------|-------------------------------|
| | Single-pollutant | Two-pollutant | Single-pollutant | Two-Pollutant | Single-Pollutant | Two-Pollutant |
| Doctor diagnosis of asthma | 0.53(0.11-2.34) ^{1a} | 0.28(0.01-2.41) ^{1b} | 0.76(0.31-2.04) ^{1c} | 0.83(0.33-1.92) ^{1d} | 0.79(0.21-3.04) ^{1e} | 0.64(0.10-2.69) ^{1f} |
| Asthma-symptom score ≥ 2* | 0.48(0.22-1.13) ^{2a} | 0.28(0.12-1.01) ^{2b} | 0.69(0.44-1.09) ^{2c} | 0.58(0.41-1.03) ^{2d} | 0.52(0.22-0.91)^{2e} | 0.39(0.21-0.93) ^{2f} |
| Self-reported chest pain | 3.04(0.73-12.27) ^{3a} | 0.87(0.16-5.14) ^{3b} | 0.76(0.43-1.76) ^{3c} | 0.74(0.34-1.49) ^{3d} | 0.88(0.31-3.17) ^{3e} | 0.48(0.11-2.13) ^{3f} |
| Self-reported hypertension | 1.00(0.44-2.83) ^{4a} | 1.49(0.44-5.71) ^{4b} | 1.12(0.63-1.88) ^{4c} | 1.08(0.63-2.01) ^{4d} | 1.03(0.37-2.40) ^{4e} | 1.00(0.8-2.71) ^{4f} |
| Self-reported high cholesterol | 1.24(0.29-5.61) ^{5a} | 0.80(0.11-5.76) ^{5b} | 0.68(0.32-1.47) ^{5c} | 0.64(0.32-1.42) ^{5d} | 0.49(0.11-2.01) ^{5e} | 0.42(0.11-1.72) ^{5f} |

Bold text denotes statistical significance at p < 0.05

Appendix H displays list of confounders included in each model

*Asthma symptom score calculated as sum of: Wheezing in the last 12 months, Shortness of breath in last 12 months, woken up by feeling of tight chest in the last 12 months, Attack of shortness of breath at rest in the last 12 months, Attack of shortness of breath after exercise in the last 12 months, Woken up by attack of shortness of breath in the last 12 months, Self-reported asthma, Medication for asthma control

Appendix H: List of confounders included in the models investigating the association between PM_{2.5} levels and cardiorespiratory outcomes

| | A | b | c | d | e | f |
|----------|---|---|--|---|---|---|
| 1 | age, sex, smoke, pet, affected by animals dust or pollen from trees or flowers | age, sex, smoke, affected by animals dust or pollen from trees or flowers | age, sex, smoke, pet, affected by animals dust or pollen from trees or flowers | age, sex, smoke, born in town, affected by animals dust or pollen from trees or flowers | age, sex, smoke | age, sex, smoke, born in town, affected by animals dust or pollen from trees or flowers |
| 2 | age, sex, smoke, brick house | age, sex, smoke, brick house, damp spots inside house in last 12 months | age, sex, smoke, brick house | age, sex, smoke, damp spots inside house in last 12 months | age, sex, smoke | Age, sex, smoke, employed, damp spots inside house in last 12 months |
| 3 | age, sex, smoke, active in past month, receiving emotional support, receiving financial support | age, sex, smoke, active in past month, receiving emotional support, receiving financial support | age, sex, smoke, receiving emotional support, receiving financial support | age, sex, smoke, active in past month, receiving emotional support, receiving financial support | age, sex, smoke, receiving emotional support, receiving financial support | age, sex, smoke, active in past month, receiving emotional support, receiving financial support |
| 4 | age, sex, smoke, receiving emotional support | Age, sex, smoke, active in past month, receiving emotional support | age, sex, smoke, active in past month, receiving emotional support | age, sex, smoke, active in past month, receiving emotional support | age, sex, smoke, active in past month, receiving emotional support | age, sex, smoke, receiving emotional support |
| 5 | age, sex, smoke, receiving financial support | Age, sex, smoke, receiving financial support | age, sex, smoke | age, sex, smoke, active in past month, receiving emotional support, receiving financial support | age, sex, smoke | age, sex, smoke, receiving financial support |

Appendix I : Journal guidelines for authors

Submissions

- » [Online Submissions](#)
- » [Author Guidelines](#)
- » [Copyright Notice](#)
- » [Privacy Statement](#)

Online Submissions

Already have a Username/Password for South African Medical Journal?

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Registration and login are required to submit items online and to check the status of current submissions.

Author Guidelines

The *SAMJ* has launched a new submission and tracking system. Authors will be required to register a profile on the Editorial Manager platform in order to submit a manuscript.

To submit a manuscript, please proceed to the *SAMJ* Editorial Manager website:

www.editorialmanager.com/samj

To access and submit an article already in production, please see the guidelines [here](#).

Author Guidelines

Please view the [Author Tutorial](#) for guidance on how to submit on Editorial Manager.

Please take the time to familiarise yourself with the policies and processes below. If you still have any questions, please do not hesitate to ask our editorial staff (tel.: +27 (0)21 532 1281, email: submissions@hmpg.co.za).

SAMJ policies

- [Types of articles considered by the SAMJ](#)
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SAMJ Policies

Type of articles considered by the SAMJ

The *SAMJ* will no longer limit the articles accepted to those that have ‘general medical content’, but is intending to capture the spectrum of medical and health sciences, grouped by relevance to the country’s burdens of disease. This content will include research in the social sciences and economics that is relevant to the medical issues around our burden of disease. Please see ‘[A new vision for the SAMJ – and a call for papers](#)’ for a full discussion of the new directions for the *SAMJ*.

We accept the following types of articles:

[Research](#)

[Reviews](#)

[Clinical trials](#)

[Editorials](#)

[In Practice](#) (Previously Forum incl. Case Reports)

[Correspondence](#)

[Obituaries](#)

[Book reviews](#)

[Ad hoc supplements](#) e.g. guidelines, conference/congress abstracts, Festschrifts*

The following articles are by invitation only:

Guest editorial

Continuing Medical Education (CME)

*Contact claudian@hmpg.co.za for information on submitting ad hoc/commissioned supplements, including guidelines, conference/congress abstracts, Festschrifts, etc.

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Queries can be directed to claudian@hmpg.co.za.

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Authorship

Named authors must consent to publication. Authorship should be based on: (i) substantial contribution to conceptualisation, design, analysis and interpretation of data; (ii) drafting or critical revision of important scientific content; or (iii) approval of the version to be published. These conditions must all be met (uniform requirements for manuscripts submitted to biomedical journals; refer to www.icmje.org)

If authors’ names are added or deleted after submission of an article, or the order of the names is changed, all authors must agree to this in writing.

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Author contributions should be listed/described in the manuscript.

Conflicts of interest

Conflicts of interest can derive from any kind of relationship or association that may influence authors’ or reviewers’ opinions about the subject matter of a paper. The existence of a conflict – whether actual, perceived or potential – does not preclude publication of an article. However, we aim to ensure that, in such cases, readers have all the information they need to enable them to make an informed assessment about a publication’s message and

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Authors must provide evidence of Research Ethics Committee approval of the research where relevant. Ensure the correct, full ethics committee name and reference number is included in the manuscript.

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As per the recommendations published by the International Committee of Medical Journal Editors (ICMJE), clinical trial research is any research that assigns individuals to an intervention, with or without a concurrent comparison/control group to study the cause-and-effect relationship between the intervention and health outcomes. All clinical trials should be registered with the appropriate national clinical trial registry (or any international primary register, if relevant), and the trial registration number should be cited at the end of the abstract. All clinical trial reports must also contain a data sharing statement as per the recommendations of the ICMJE. Statements are to indicate:

- whether individual deidentified participant data will be shared;
- what data in particular will be shared; whether additional, related documents will be available;
- when the data will become available and for how long; by what access criteria data will be shared.

Please see the ICMJE announcement for further details and illustrative examples of data sharing statements: [ICMJE Data Sharing Statements for Clinical Trials](#)

Since 1st December 2005, all clinical trials conducted in South Africa have been required to be registered in the South African National Clinical Trials Register. The SAMJ therefore requires that clinical trials be registered in the relevant public trials registry at or before the

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Please refer to the general guidelines for all papers at the top of this article for additional requirements with respect to ethics approval, funding, author contributions, etc. The format of original research articles should be followed for reporting of clinical trial results.

Patient Consent

Information that would enable identification of individual patients should not be published in written descriptions, photographs, and pedigrees unless the information is essential for scientific purposes and the patient (or parent or guardian) has given informed written consent for publication and distribution. We further recommend that the published article is disseminated not only to the involved researchers but also to the patients/participants from whom the data was drawn. Refer to Protection of Research Participants. The signed consent form should be submitted with the manuscript to enable verification by the editorial team.

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Manuscript preparation

Preparing an article for anonymous review

To ensure a fair and unbiased review process, all submissions are to include an anonymised version of the manuscript. The exceptions to this are Correspondence, Book reviews and Obituary submissions.

Submitting a manuscript that needs additional blinding can slow down your review process, so please be sure to follow these simple guidelines as much as possible:

- An anonymous version should not contain any author, affiliation or particular institutional details that will enable identification.
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General article format/layout

Accepted manuscripts that are not in the correct format specified in these guidelines will be returned to the author(s) for correction, which will delay publication.

General:

- Manuscripts must be written in UK English.
- The manuscript must be in Microsoft Word format. Text must be single-spaced, in 12-point Times New Roman font, and contain no unnecessary formatting (such as text in boxes).
- Please make your article concise, even if it is below the word limit.
- Qualifications, **full** affiliation (department, school/faculty, institution, city, country) and contact details of ALL authors must be provided in the manuscript and in the online submission process.
- Abbreviations should be spelt out when first used and thereafter used consistently, e.g. 'intravenous (IV)' or 'Department of Health (DoH)'.
- Include sections on Acknowledgements, Conflict of Interest, Author Contributions and Funding sources. If none is applicable, please state 'none'.
- Scientific measurements must be expressed in SI units except: blood pressure (mmHg) and haemoglobin (g/dL).
- Litres is denoted with an uppercase L e.g. 'mL' for millilitres).
- Units should be preceded by a space (except for % and °C), e.g. '40 kg' and '20 cm' but '50%' and '19°C'.
- Please be sure to insert proper symbols e.g. μ not u for micro, α not a for alpha, β not B for beta, etc.
- Numbers should be written as grouped per thousand-units, i.e. 4 000, 22 160.
- Quotes should be placed in single quotation marks: i.e. The respondent stated: '...'
- Round brackets (parentheses) should be used, as opposed to square brackets, which are reserved for denoting concentrations or insertions in direct quotes.
- If you wish material to be in a box, simply indicate this in the text. You may use the table format –this is the *only* exception. Please DO NOT use fill, format lines and so on.

SAMJ is a generalist medical journal, therefore for articles covering genetics, it is the responsibility of authors to apply the following:

- Please ensure that all genes are in italics, and proteins/enzymes/hormones are not.
- Ensure that all genes are presented in the correct case e.g. TP53 not Tp53.

****NB:** Copyeditors cannot be expected to pick up and correct errors wrt the above, although they will raise queries where concerned.

- Define all genes, proteins and related shorthand terms at first mention, e.g. '188del11' can be glossed as 'an 11 bp deletion at nucleotide 188.'
- Use the latest approved gene or protein symbol as appropriate:

- Human Gene Mapping Workshop (HGMW): genetic notations and symbols
- HUGO Gene Nomenclature Committee: approved gene symbols and nomenclature
- OMIM: Online Mendelian Inheritance in Man (MIM) nomenclature and instructions

- Bennet et al. Standardized human pedigree nomenclature: Update and assessment of the recommendations of the National Society of Genetic Counselors. J Genet Counsel 2008;17:424-433: standard human pedigree nomenclature.

Preparation notes by article type

- Research
- Editorials
- CME
- In Practice and Case reports
- Reviews
- Clinical trials
- Correspondence
- Obituaries
- Book reviews
- Guidelines

Research

Guideline word limit: 4 000 words

Research articles describe the background, methods, results and conclusions of an original research study. The article should contain the following sections: introduction, methods, results, discussion and conclusion, and should include a structured abstract (see below). The introduction should be concise – no more than three paragraphs – on the background to the research question, and must include references to other relevant published studies that clearly lay out the rationale for conducting the study. Some common reasons for conducting a study are: to fill a gap in the literature, a logical extension of previous work, or to answer an important clinical question. If other papers related to the same study have been published previously, please make sure to refer to them specifically. Describe the study methods in as much detail as possible so that others would be able to replicate the study should they need to. Results should describe the study sample as well as the findings from the study itself, but all interpretation of findings must be kept in the discussion section, which should consider primary outcomes first before any secondary or tertiary findings or post-hoc analyses. The conclusion should briefly summarise the main message of the paper and provide recommendations for further study.

Select figures and tables for your paper carefully and sparingly. Use only those figures that provided added value to the paper, over and above what is written in the text.

Do not replicate data in tables and in text .

Structured abstract

- This should be 250-400 words, with the following recommended headings:
 - **Background:** why the study is being done and how it relates to other published work.
 - **Objectives:** what the study intends to find out
 - **Methods:** must include study design, number of participants, description of the intervention, primary and secondary outcomes, any specific analyses that were done on the data.

- **Results:** first sentence must be brief population and sample description; outline the results according to the methods described. Primary outcomes must be described first, even if they are not the most significant findings of the study.
- **Conclusion:** must be supported by the data, include recommendations for further study/actions.
- Please ensure that the structured abstract is complete, accurate and clear and has been approved by all authors.
- Do not include any references in the abstracts.

Here is an example of a good abstract.

Main article

All articles are to include the following main sections: Introduction/Background, Methods, Results, Discussion, Conclusions.

The following are additional heading or section options that may appear within these:

- Objectives (within Introduction/Background): a clear statement of the main aim of the study and the major hypothesis tested or research question posed
- Design (within Methods): including factors such as prospective, randomisation, blinding, placebo control, case control, crossover, criterion standards for diagnostic tests, etc.
- Setting (within Methods): level of care, e.g. primary, secondary, number of participating centres.
- Participants (instead of patients or subjects; within Methods): numbers entering and completing the study, sex, age and any other biological, behavioural, social or cultural factors (e.g. smoking status, socioeconomic group, educational attainment, co-existing disease indicators, etc) that may have an impact on the study results. Clearly define how participants were enrolled, and describe selection and exclusion criteria.
- Interventions (within Methods): what, how, when and for how long. Typically for randomised controlled trials, crossover trials, and before and after studies.
- Main outcome measures (within Methods): those as planned in the protocol, and those ultimately measured. Explain differences, if any.

Results

- Start with description of the population and sample. Include key characteristics of comparison groups.
- Main results with (for quantitative studies) 95% confidence intervals and, where appropriate, the exact level of statistical significance and the number need to treat/harm. Whenever possible, state absolute rather than relative risks.
- Do not replicate data in tables and in text.
- If presenting mean and standard deviations, specify this clearly. Our house style is to present this as follows:
- E.g.: The mean (SD) birth weight was 2 500 (1 210) g. Do not use the \pm symbol for mean (SD).

- Leave interpretation to the Discussion section. The Results section should just report the findings as per the Methods section.

Discussion

Please ensure that the discussion is concise and follows this overall structure – sub-headings are not needed:

- Statement of principal findings
- Strengths and weaknesses of the study
- Contribution to the body of knowledge
- Strengths and weaknesses in relation to other studies
- The meaning of the study – e.g. what this study means to clinicians and policymakers
- Unanswered questions and recommendations for future research

Conclusions

This may be the only section readers look at, therefore write it carefully. Include primary conclusions and their implications, suggesting areas for further research if appropriate. Do not go beyond the data in the article.

Editorials

Guideline word limit: 1 000 words

These opinion or comment articles are usually commissioned but we are happy to consider and peer review unsolicited editorials. Editorials should be accessible and interesting to readers without specialist knowledge of the subject under discussion and should have an element of topicality (why is a comment on this issue relevant now?) There should be a clear message to the piece, supported by evidence.

Please make clear the type of evidence that supports each key statement, e.g.:

- expert opinion
- personal clinical experience
- observational studies
- trials
- systematic reviews.

CME (by invite only)

CME is intended to provide readers with practical, up-to-date information on medical and related matters. It is aimed at those who are not specialists in the field.

From January 2016, all CME articles will be printed in full in the *SAMJ*. Please try to adhere strictly to the guidelines on word count as we have a page limit for the print issue of the *SAMJ*. We reserve the right to place some tables and reference lists online if this is necessary for space.

In practice, this means that each CME topic usually covers two issues of the print issue of the *SAMJ*.

The guest editor, in consultation with the editor, is responsible for convening a team of authors, deciding on the subjects to be covered and for reviewing the manuscripts submitted. The suggestion is for 4 - 5 articles, although there is some room for flexibility contingent on discussions with the editor.

For queries about these guidelines please feel free to contact the CME editor, Dr Bridget Farham, by email (ugqirha@iafrica.com) or telephone (+27 (0)21 789 2331).

Review process

The guest editor reviews the articles and returns them to the CME editor for review and final approval.

Guest editorials

Guideline word limit: 1 000 words

- Include the guest editor's personal details (qualifications, positions, affiliation, e-mail address, and a short personal profile (50words)).
- If possible, include a photograph of the author(s) at high enough resolution for print. It is preferable to provide two guest editorials, one for each issue, so that the content of the articles in each issue is covered.

Articles

Guideline word limit: 2 000 - 3 000 words

- Each article requires an abstract of ± 200 words.
- The editor reserves the right to shorten articles but will send a substantially shortened article back for author approval.

Personal details

Please supply: Your qualifications, position and affiliations and MP number (used for CPD points); Address, telephone number and fax number, and your e-mail address; and a short personal profile (50words) and a few words about your current fields of interest.

In Practice

Guideline word limit: 2 000 - 3 000 words

This section includes articles that would previously have been accepted into the Forum section, and case reports.

In practice articles are those that draw attention to specific issues of clinical, economic or political interest regarding medicine and healthcare in southern Africa. They are assigned to a topic:

Case report
Clinical practice
Clinical alert
Issues in medicine
Issues in public health
Healthcare delivery
Consensus/Position statement
Medicine and the environment
Medicine and the law
Cochrane corner

An In Practice article should follow the following format – sub-headings are not necessary, but may be used for clarity:

- Author affiliations and qualifications: to be the same as for Research. Provide all authors' names and initials, qualifications and full affiliations, and corresponding author.
- Short abstract: does not need to be structured, but should capture the essential features of the article
- Introduction: the reason for the article and the issue being addressed
- Recent research, discussion, local policy around the issue – include your own research where appropriate
- All statements should be referenced and, if opinion only, this should be stated
- Discussion: how this article adds to the discussion around a particular topic
- If a clinical practice or policy point is at issue, this needs to be emphasised, using a box with highlights if appropriate.

Essentially In practice is an opportunity for a more discursive approach to topics of clinical, economic or political importance in southern African health systems. It is not an opportunity to put forward unsubstantiated opinions!

Case reports

The *SAMJ* has recently started to accept case reports. The cases must come from Africa, preferably southern Africa unless the condition is common to all African countries, and must be either a completely new description of a clinical condition or result (use Google!) or a case that highlights important practice or management issues.

Please use the following format for case reports:

- Title of case: do not include the words 'a case report' in the title
- Summary/abstract: up to 150 words summarising the case presentation and outcome
- Background: why is this case important and why did you write it up?
- Case presentation: presenting features, medical, social, family history as appropriate
- Case management: should be according to best practice, and if not, please explain why
- Investigations, if relevant: save space by simply saying 'normal' if, for example, renal function was completely normal, rather than listing normal results, highlight the abnormal – or indeed the normal if this is clinically significant

- Differential diagnosis, if relevant
- Treatment, if relevant
- Outcome and follow-up
- Discussion – a VERY BRIEF review of similar published cases
- Teaching points: 3 - 5 bullet points
- References: as per the *SAMJ* house style
- Tables and figures: keep to a minimum. Use clinical images where relevant – we need hi-res versions for print, and identifiable persons must have a consent form
- Patient consent: please include a statement about patient consent to a written case report. This should be uploaded as a supplementary file.